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In Memoriam

ARCHIBALD YOUNG
(1873-1939)

IT is with regret that we have to announce the death of Professor Archibald Young, which took place on July 23 at his residence in Glasgow.

For a number of years he had been handicapped by indifferent health. In spite of that he worked without remission till the spring of this year, when he was forced to realize that his strength was failing—a fact already patent to his many friends and colleagues. Under the age limit he was due to retire from his Chair on September 30, but he did not live to complete his tenure of office. Like Macleod and Macewen, his immediate predecessors in the Chair, he died in harness. For a considerable time he had suffered pain. Life for him had truly become a 'fitful fever' against which he had battled manfully. When the end came he went down with colours flying.

Archibald Young was born in Glasgow in 1873. His forebears were Glasgow citizens, and he himself, continuing the tradition of several generations, was in due course admitted a burgess of that city. After completing his preliminary education in the High School he proceeded to the University of Glasgow, where in 1893 he graduated B.Sc., and in 1895 M.B., C.M., 'with high commendation'. After holding the usual resident posts in hospital he obtained one of the junior surgical appointments in the Western Infirmary, and served for some time as university assistant to the late Professor Sir William Macewen. Passing through the successive intermediate grades of the staff, he ultimately became in 1917 one of the visiting surgeons to the hospital, a post which he held till his death. While still a junior he had commenced teaching extramural classes, and in 1913 was appointed Professor of Surgery in Anderson's College. In the same year he took the fellowship of the Royal Faculty of Physicians and Surgeons.

Early association with his teacher, Macewen, naturally directed his attention to surgical neurology and gave him the opportunity of still further developing the faculty for unending hard work, a characteristic which had already shown itself in his undergraduate years. On the death of Macewen, Young was in 1924 appointed to succeed him as Regius Professor of Surgery in the University.

The successor of a man of the calibre of Macewen has always a hard furrow to plough. Young bent himself to the task. The responsible duties of the Chair were discharged by him conscientiously and well. The teaching of large classes

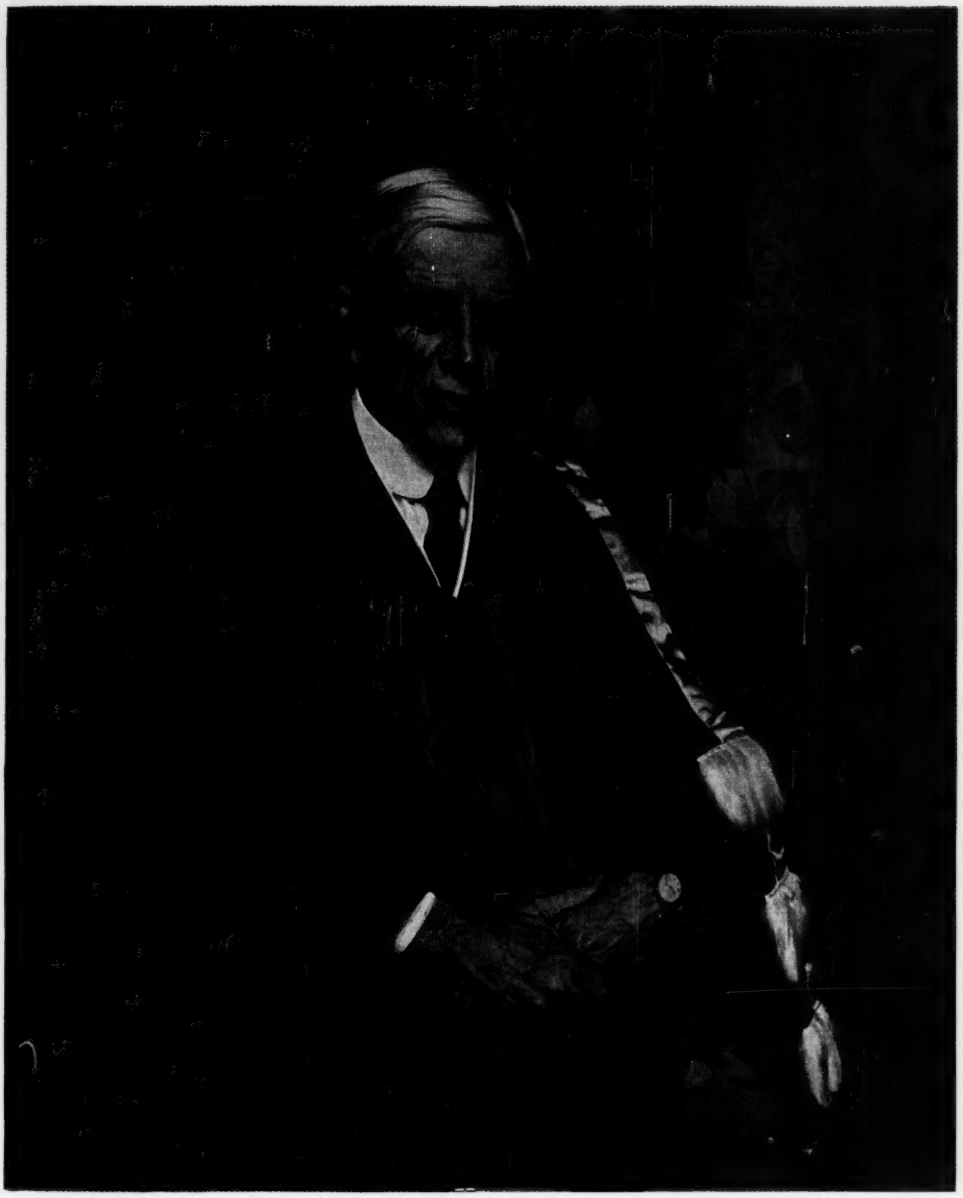
was carefully organized, a museum of surgical pathology was built up and was constantly being added to, and from time to time he contributed to surgical literature papers on such subjects as the operative treatment of fractures, the injuries of peripheral nerves, cerebral surgery, and the surgery of the sympathetic nervous system. His last literary work—translating and editing Leriche's *Surgery of Pain*—was completed in the early months of this year, latterly from a sickbed.

In his clinical work Young was cautious but progressive. Mere novelty in a method or a policy did not appeal to him and he would advocate or agree to it only if after due consideration and experience he became convinced of its soundness.

His writings attracted attention far beyond the confines of the United Kingdom, and he was a frequent visitor to European and American clinics. He was the recipient of many honorary distinctions in surgery—M.D. Strasbourg, Fellowship of the American College of Surgeons and of the Academy of Surgery of Philadelphia, Membership of the Academy of Medicine of Rome and of the French Academy of Surgery. He was President of the Association of Surgeons of Great Britain and Ireland, 1926–27, and of the Royal Faculty of Physicians and Surgeons of Glasgow, 1935–37. His public work at home was recognized by his being appointed a Justice of the Peace and a Deputy-Lieutenant of the County of the City of Glasgow.

Professor Young had been a member of the Editorial Committee of the BRITISH JOURNAL OF SURGERY since 1928 and afforded valuable help and advice.

He leaves a widow, and two sons, of whom the elder is a member of the profession in which his father occupied an honoured position.



ARCHIBALD YOUNG

1873—1939

From a painting by James Gunn, and reproduced by permission of the Glasgow University Court

AN INVESTIGATION INTO THE EFFECTS OF RADIUM UPON CARCINOMA OF THE BREAST*

By J. PATERSON ROSS

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THE REASON FOR THE INVESTIGATION

THE radium treatment of operable carcinoma of the breast by the method which has since become known as the "Keynes technique" was started in the Surgical Professorial Unit at St. Bartholomew's Hospital in 1924. This was done only after a preliminary trial of the method in treating cases of inoperable or recurrent carcinoma had yielded results which were so encouraging that Professor George Gask and Mr. Geoffrey Keynes were led to believe that their patients were running no additional risk by submitting to radium treatment instead of radical mastectomy. Our subsequent experience has amply justified their faith.

It was one of the first duties of the newly established Follow-up Department at St. Bartholomew's to keep in touch with all patients suffering from carcinoma of the breast, whether treated by radium or mastectomy, and after a few years it became apparent that the percentage survival rates of the two groups were almost identical. Lest the surgery at St. Bartholomew's be criticized as a standard of comparison, I have taken figures for radical mastectomy without irradiation published by Mr. Gordon-Taylor (1938) and by Mr. J. L. Joyce (1937), and plotted them on a graph with those for radium treatment by Mr. Keynes (1937) and by the Surgical Professorial Unit at St. Bartholomew's (*Fig.* 145). Radium figures are sometimes criticized as representing the work of the expert; the Surgical Unit figures show the results obtained by eight surgeons, and though, in comparison with Mr. Keynes's own results, they reflect to some extent the errors of inexperience, yet they do not fall far short of the achievements of very expert surgery, and are considerably better than most hospital statistics.

But as the patients returned regularly for re-examination we were soon faced with the problem of the swelling which frequently remained at the tumour site after radium had been applied. In many cases this lump diminished in size, gradually becoming softer and less definite, and was clearly attributable to fibrosis—the process of resolution of the tissue reaction to the cancer cells, and later to the radium, being rather prolonged.

In other cases, the swelling, which was insignificant shortly after irradiation, became larger and firmer; and, particularly when its appearance was delayed for many months, persistent growth was so strongly suspected that we were forced to excise a number of these swellings to see what they were. We found that although about half of them contained carcinoma cells, the remainder showed only dense scar tissue, and we noted that among the latter group there were several cases in which a heavy dose of radium had been used. Since the most

* Hunterian Lecture delivered at the Royal College of Surgeons of England, January 18, 1939.

careful study of these cases failed to give us any clinical criterion whereby we might distinguish the innocent from the malignant residual swellings, we decided that the frequency of the persistence of carcinoma cells at the tumour site after radium treatment could be determined only by the routine clinical and histological examination of a series of cases treated as far as possible by a standard method.

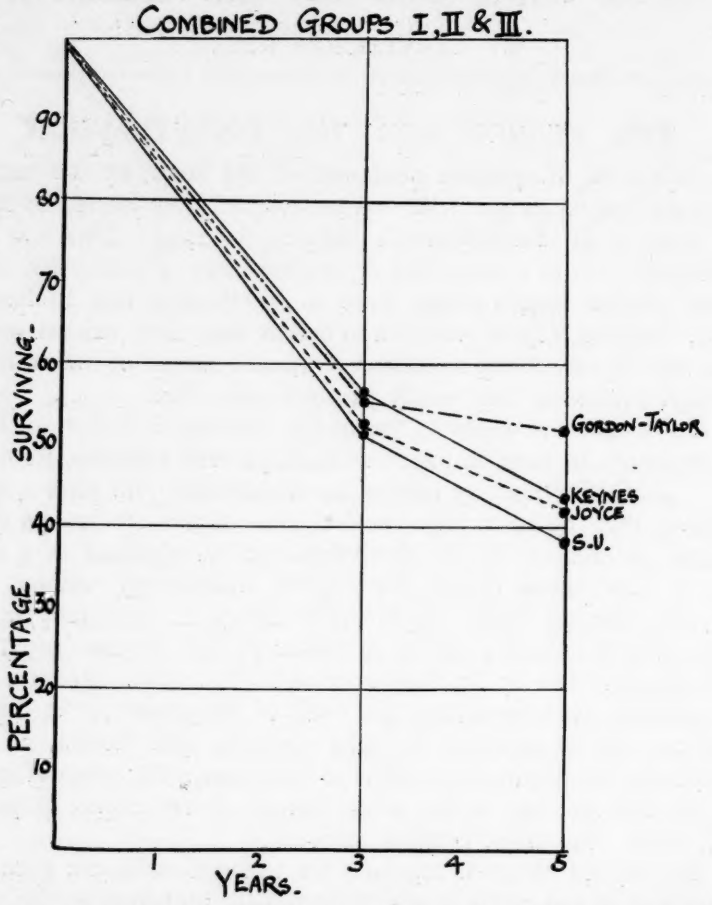

FIG. 145.—Graph showing 3-year and 5-year survival rates published by Mr. Gordon-Taylor, Mr. Joyce, and Mr. Keynes, and also those recorded by the Surgical Professorial Unit at St. Bartholomew's Hospital. The figures refer to the total numbers of cases treated, irrespective of the stage of the disease (Groups I, II, and III combined).

Before proceeding to describe the work I would like to say that we are now satisfied that our patients have not been exposed to any additional risk as the subjects of this critical therapeutic experiment—in fact we have evidence that they may even have benefited to an appreciable extent by the modifications in treatment which the new routine involved.

THE METHOD OF INVESTIGATION

1. Selection of Cases.—Since we were anxious to discover the effects of radium upon the *average* case of carcinoma of the breast, there was no deliberate selection of those cases which seemed particularly suitable for this form of

treatment. We knew from our previous experience that the presence of much fat in the breast, or of lymphatic œdema over it, with an ill-defined tumour, were unfavourable features; but since the influence of these factors upon the results of amputation of the breast is also bad, we did not consider that we were exposing our patients to an additional risk by treating them all with radium in a continuous series. Every patient, however, was told what radium treatment would mean and was allowed to choose between irradiation and radical amputation. The few who preferred amputation were the only ones who broke the continuous series of what must be regarded as 'unselected' cases.

2. Preliminary Examination and Records.—When the clinical examination had been completed the breast tumour was outlined on the skin with Indian ink, other marks were made to indicate the size and position of axillary metastases, and the patient was then photographed. The photograph was subsequently pasted into a book with pages large enough to take the complete record of one patient on each page.

The clinical notes referred only to the points which we considered to be the most important—the patient's age, the length of the history, presence of a discharge from the nipple, the measurements of the breast tumour and its attachments to the skin or pectoral fascia, and the number and size of the palpable glands in the axilla.

3. Irradiation.—Radium needles were inserted following a uniform technique. The needles contained either 3 mg. or 2 mg. of radium (active length 4·8 cm. and 3·2 cm. respectively) filtered by either 0·5 mm. of platinum in the earlier cases, or 0·8 of platinum later in the series. The 3-mg. needles were placed just deep to the tumour (not into it) so as to irradiate it from its deep aspect; upon the pectoral fascia to irradiate the whole breast from below; in the axilla along the chest wall, converging towards the apex and reaching as high as possible; and below the clavicle, being passed through pectoralis major muscle to lie upon the costocoracoid membrane. Needles were always placed in this position, and in almost all cases 2-mg. needles were inserted into the upper four or five intercostal spaces at their anterior ends (the points of the needles being in contact with the border of the sternum), and also above the clavicle in the posterior triangle of the neck, but we have come to doubt the value of these last two groups of needles.

At some convenient time during the subsequent week a radiograph was made for record purposes to show the position of the needles.

4. Removal of Radium and Biopsy.—After the needles had been in position for seven days they were removed, and at the same time a small piece of the tumour was excised for histological examination. Microphotographs were made to record the morphological type of the neoplasm.

The patient was then examined at monthly intervals, and was re-admitted to hospital for excision of the breast and axillary contents at a definite period after irradiation—in the first 50 cases the period was three months, and in the remaining 22 cases six months. Careful notes of the state of the breast and axilla were made at each examination and also when the patient returned for operation.

5. Excision of the Breast.—In performing the excision a conservative operation was carried out, the pectoral muscles being left behind. The breast and pectoral fascia were removed, and the fat and glands were cleared out of the axilla as completely as the presence of the muscles permitted. Though this is

admittedly an inadequate operation, we felt that it was sufficient when combined with the preliminary irradiation, and we are satisfied that we have been able in all cases to remove the axillary contents cleanly enough to avoid vitiating the results of the clinical experiment by leaving infected glands behind. Preservation of the muscles has prevented operative shock and diminished subsequent deformity, and our experience has shown that the patients have not been running an undue risk, and may even have benefited somewhat in comfort and in bodily activity, by our conservatism.

After operation the patients continue to be examined at intervals of three months.

6. Examination of the Tissue Excised.—The excised tissue was carefully plotted out like a map, so that sections taken from any part might be identified. The whole breast was then sliced in every case, and specimens were taken for histological study from the original tumour site and from any enlarged glands in the axillary fat, microphotographs being made as required.

In the earlier cases of the series we marked the tumour by means of an empty radon-seed container, but subsequent examination of the specimens proved that this was unnecessary. Also in the earliest cases we went methodically through the whole of the breast tissue searching for secondary centres of malignant disease, but as we never found any this part of the investigation was given up.

THE RESULTS OF THE INVESTIGATION

Since most of our observations have been made on cases in which the breast was removed three months after the insertion of radium, the expression "after irradiation" should be taken to refer to this three-months' period unless the time interval is specially stated.

A. CLINICAL RESULTS

1. Breast.—In 37 out of the 50 cases in the first series a lump was still palpable in the breast three months after irradiation. Often it was considerably smaller, and its outlines might be less definite, but it was there. Of these 37 lumps 23 contained carcinoma cells, the remaining 14 consisting merely of scar tissue.

2. Axillary Glands.—Any glands palpable at the time the breast was excised were found to be carcinomatous. But in 16 cases in which the glands could not be felt before operation deposits of carcinoma were found on microscopic examination.

Initially 32 out of the 50 patients had palpable glands, but many more may have had carcinomatous glands. In 17 of these 32 patients the glands could no longer be felt after irradiation, and the specimens were proved to be free from carcinoma. Among the remaining 15 cases in which the glands were found to be carcinomatous after irradiation, they were palpable in 6, but could not be felt in 9 cases.

These figures are quoted partly to show the satisfactory results obtainable by radium treatment of the axilla, but also to indicate how fallacious the grouping of cases according to the stage of the disease may be when this is done on a clinical basis. For statistical purposes grouping on a pathological basis is the only satisfactory method.

3. Survival Rate.—The investigation was started at the end of 1932. The result as estimated by the survival rate gives a three-year rate of 50 per cent

—without any allowance being made for the fact that several of the patients are known to have died of diseases other than carcinoma of the breast. Of the 13 patients treated over five years ago, 6 are still alive and well. There was no operative mortality.

B. HISTOLOGICAL STUDIES

1. Breast.—

a. Three Months' Series.—The carcinoma, when present at all, was found only near the site of the primary tumour, no secondary foci of growth being found in other parts of the breast.

It has been mentioned already that 27 out of the 50 specimens contained carcinoma cells, but not all of them appeared to be capable of further activity. Whenever cell outlines and nuclei were visible the section was considered to be positive, but by studying the staining reactions an attempt was made to subdivide the positives into those with active cells and those in which the cells showed degenerative changes.

Histological examination showed that the tumours varied considerably in their cellular pattern, and the majority were found to belong to one of four types. A few could not be classified in this way, and will be referred to separately later on. It is our impression that these types vary in their sensitivity to irradiation, and if this variation can be established, its influence upon the problem of radium treatment calls for careful consideration.

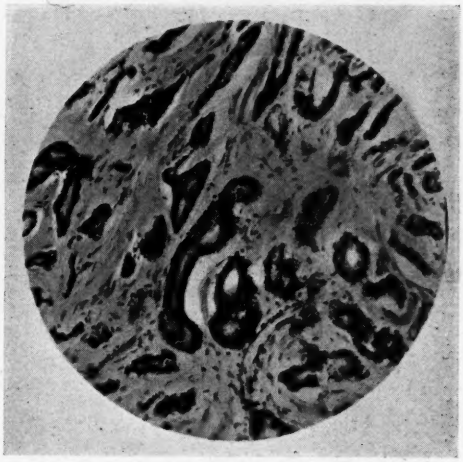

FIG. 146.—Showing the well-differentiated type of carcinoma of the breast referred to as adenocarcinoma. Note the appearance of acinus and duct formation. Specimen taken before irradiation.

Adenocarcinoma: In this type the cells show clearly an attempt at acinus or duct formation, approximating more closely than any other carcinoma to the appearances of the normal breast (*Fig.* 146). The growth is moderately cellular, the groups of cells are not very large, and there is a considerable quantity of fibrous tissue laid down between the collections of epithelial cells. The arrangement of a single layer of regular cells around a central lumen is frequently seen, and there is little tendency to degenerative change in the tumour.

Of our 50 cases 7 belonged to this type, and after irradiation only 1 was found to be negative; but of the 6 positives 3 showed a good deal of degeneration, though the remaining 3 contained active-looking carcinoma.

On following up these cases, however, 6 out of the 7 patients are now alive, and it would appear that this type of tumour, though rather insensitive to radium, is not very malignant. Its tendency to reproduce the features of normal breast tissue supports this estimate of its character.

Carcinoma simplex: Here the cells are arranged in an alveolar formation, but without bearing any resemblance to the normal breast (*Fig.* 147). The epithelial cellular elements predominate in that they are aggregated into large clusters of

cells many of which show signs of active division and growth, and the fibrous tissue is comparatively small in amount.

Though this type may be considered to represent the standard carcinoma of the breast, it is curious that in this series there are only 5 cases belonging to it.

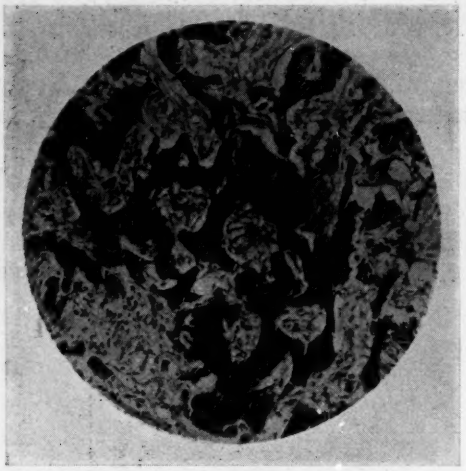

FIG. 147.—Carcinoma simplex. Alveolar arrangement of cells without any resemblance to normal breast. Specimen taken before irradiation.

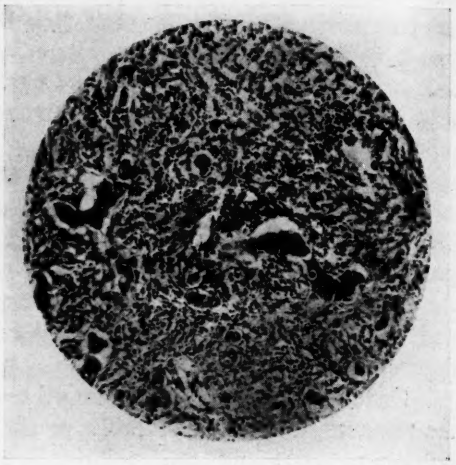

FIG. 148.—Carcinoma simplex after irradiation, showing intense leucocytic infiltration around degenerate carcinoma cells.

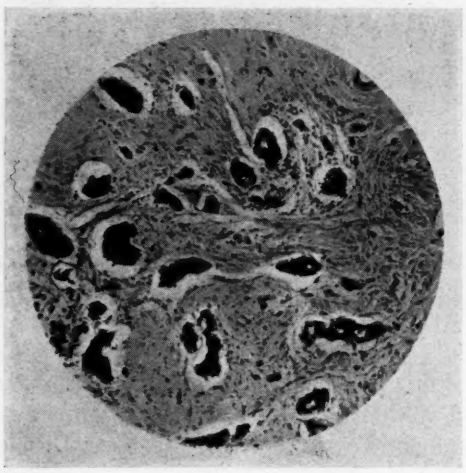

FIG. 149.—Carcinoma simplex after irradiation, showing a less cellular and more fibrotic type of growth.

FIG. 150.—Scirrhous carcinoma showing strands of cells extending beyond the breast into the subcutaneous tissue.

After irradiation 1 case was negative, and 3 out of the 4 positives showed well-marked degeneration. A prominent feature was the intense leucocytic infiltration surrounding some of the degenerate carcinoma cells, suggesting active phagocytosis of the cell debris (*Fig.* 148). Other specimens showed a less cellular and more fibrotic type of growth after irradiation (*Fig.* 149).

Of the 5 patients affected by this type of growth 3 are alive, and we may infer that it represents a moderately malignant and also moderately radiosensitive carcinoma.

Scirrhous carcinoma: The prominent feature in this type is the fibrous tissue, and the carcinoma cells which are lying in small groups or rows between the fibrous layers seem at first sight to be comparatively insignificant and almost crushed out of existence by them (*Fig.* 150). Further examination, however, shows that the growth is very widespread and many of our specimens show infiltration outside the breast tissue proper, even though the history of the presence of the lump may have been very short. This evidence of active growth, coupled with the lack of any resemblance to breast tissue or even of an 'alveolar' arrangement of the carcinoma cells, indicates a more malignant type of neoplasm, and it seems to be more sensitive to irradiation than the adenocarcinoma or the carcinoma simplex.

Of the 15 cases of this type in our series, after irradiation 7 specimens were negative, 3 showed degenerate carcinoma cells, and 5 active growth. In spite of the fact that 7 out of the 15 cases were free from growth, only 5 out of the 15 are still alive—another point indicating the malignancy of this type.

FIG. 151.—Carcinoma consisting of masses of large very active-looking cells with little fibrous tissue intervening. Collections of blood and organizing clot within the groups of carcinoma cells.

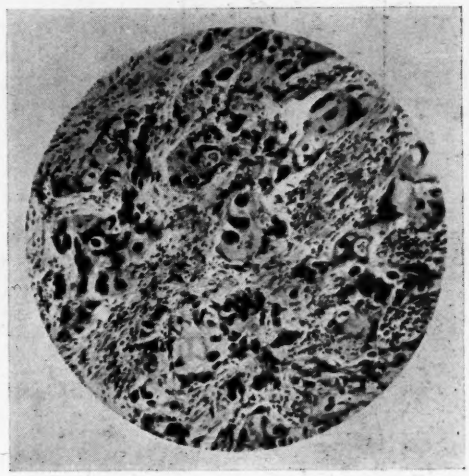

FIG. 152.—Carcinoma (unclassified) composed of large anaplastic cells.

Cellular and hæmorrhagic type: We were surprised to find that 14 out of our 50 specimens showed a type of growth in which there were large masses of very active-looking carcinoma cells lying in a matrix of rather delicate and poorly developed fibrous tissue. In the centre of many of the aggregations of carcinoma cells there were cavities filled with blood or organizing blood-clot (*Fig.* 151). The histological picture corresponds to the description of duct carcinoma in some text-books, and certainly a few of our patients with this type of growth had had a blood-stained discharge from the nipple. In most of our cases, however, the history was short, the tumour was growing quickly, and in 10 out of 14 the axillary glands were involved—all these features being unlike the behaviour of the growth commonly referred to as a duct carcinoma.

There were 14 growths of this type. After irradiation 7 specimens were free from growth, 6 showed grossly degenerated carcinoma cells, the remaining specimen being the only one having active growth in it. Yet only 4 of the 14 patients

represented are alive, and this last type is to be regarded as the most malignant and the most radiosensitive of the four we have described.

We were unable to classify 9 of our cases in these four types, either because of unsatisfactory biopsy material or because of unusual histological appearances—for example, one specimen contained extraordinary looking, large, and anaplastic cells which seemed to have no special arrangement (*Fig.* 152)—and there was one colloid carcinoma. The anaplastic growth responded well to radium and the patient is alive; the patient with the colloid carcinoma, on the other hand, died with widespread metastases in the skeleton.

It must be noted that the four types now described were those which seemed to us to stand out clearly in this series—a pathologist might make still further

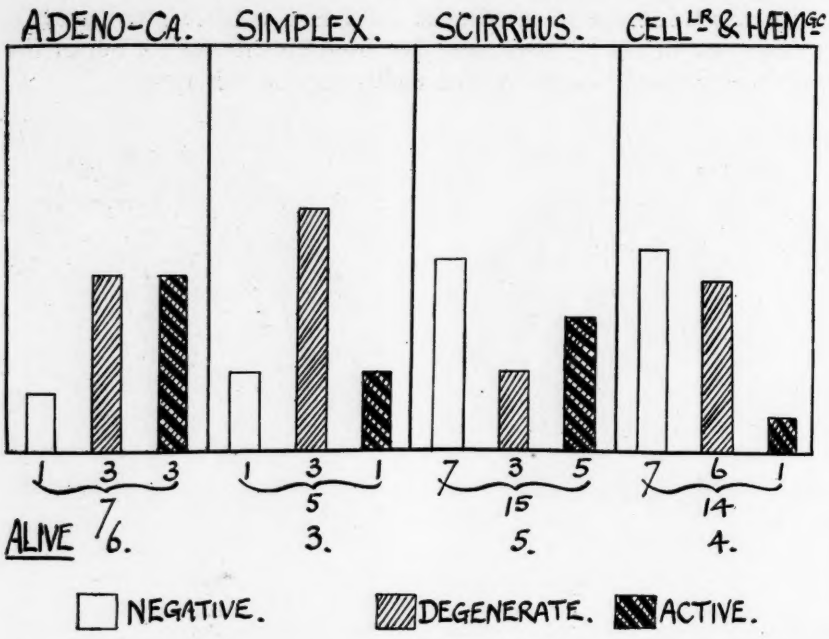

FIG. 153.—Chart showing the variation in the response to radium treatment among the four types of carcinoma classified histologically. Numbers refer to the cases in the series examined three months after irradiation with radium needles.

subdivisions, yet it is doubtful whether this degree of refinement would be helpful. Many of our specimens seemed to show portions which merged from one type into another, and we have placed them according to the predominating growth pattern. We have no desire to make extravagant claims for the accuracy of this classification, and especially we would mention that the proportional representation of the various types in this series is quite fortuitous—in fact the proportions in our 6-months' series were entirely different. All we wish to point out is that there is a degree of variation in the type of carcinoma of the breast which is sufficient to influence the malignancy of the growth and its response to radium (*Fig.* 153). The inferences drawn from a short series of cases, varying both as regards the stage of the disease and the histological type of the growth, must therefore be accepted with proper reserve.

b. Six-Months' Series.—Unfortunately the proportions of the various types of growths do not correspond with the 3-months' series—there were more of the carcinoma simplex and the adenocarcinoma types and fewer of the scirrhous and the cellular-hæmorrhagic varieties. Assuming that our former impressions were correct, the 6-months' series thus contains a higher proportion of the more radio-resistant types, as shown in the table.

TABLE SHOWING THE RESULTS OF RADIUM TREATMENT IN RELATION TO THE TYPE OF GROWTH
(20 cases of the 6-months' series which were classified histologically)

HISTOLOGICAL TYPE	NEGATIVE	DEGENERATE	ACTIVE	TOTAL
Adenocarcinoma	1	0	3	4
Carcinoma simplex	4	1	5	10
Scirrhous carcinoma	3	0	0	3
Cellular and hæmorrhagic	2	0	1	3

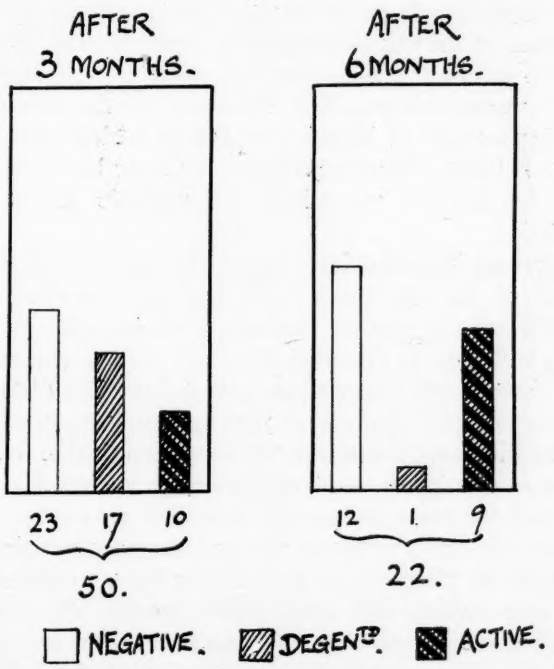

FIG. 154.—Charts to show the findings in 50 cases of carcinoma of the breast three months after irradiation, and in 22 cases six months after irradiation, with radium needles.

The most interesting observation in the histological examination of specimens six months after irradiation is the almost complete absence of those containing degenerate cells—those found after three months must either have degenerated completely and been removed, or else have become active again. Comparing the totals of 'Negative', 'Degenerate', and 'Active' growths in our 3-months' and

6-months' series we find that both the 'Negative' and the 'Active' categories have increased in the latter series at the expense of the 'Degenerate' (*Fig.* 154); but it is probable that the large proportion of 'Active' growths six months after irradiation may be related to the relative increase in the number of radioresistant growths in this series.

2. Axillary Glands.—It is impossible to tell the number of cases in which carcinoma in the axillary glands was destroyed by radium. It has been stated already that 32 out of the 50 patients had palpable enlargement of the axillary glands before irradiation, and that in 17 of these the glands could not be felt, and histological examination revealed no carcinoma after radium treatment.

On the other hand, carcinoma cells were found in the axillary glands in 14 out of the 50 cases, and we have reason to believe that in these particular cases an adequate dose of radium had been inserted into the axilla. Furthermore, whenever carcinoma cells were found in the glands they were always active looking, whether three months or six months after irradiation.

It is our impression that, as in the primary growths, the most rapidly growing deposits in the glands are the most radiosensitive, and we have made particular note of a few cases in which large masses in the axilla have been completely destroyed by radium. In one case the result was so striking—a large mass in the breast and a very large deposit in the axillary glands having disappeared clinically, and showing no trace of growth histologically three months after irradiation—that we were inclined to doubt the diagnosis, especially as the biopsy of the primary growth had been unsatisfactory. The virulence of the carcinoma was proved, however, by the appearance of hepatic metastases which proved fatal within the following year. It is likely, therefore, though we have been unable to bring direct evidence to prove it, that the metastases in lymphatic glands also vary in their response to irradiation.

3. Tissue Surrounding the Growth.—The state of the connective tissue in the neighbourhood of the carcinoma cells has an important bearing upon the effects of irradiation—the deleterious influences of infection or of an overdose of radium itself being sufficient to illustrate this fact. Our attention has been directed principally to the cancer cells themselves, and it has been difficult for us to form any proper estimate of the changes in the surrounding tissues, though special staining methods might reveal much that we have been unable to recognize. Nevertheless we have noted the aggregations of leucocytes around degenerating carcinoma cells (*Fig.* 148), and we have frequently observed an extensive laying down of fibrous tissue which has either replaced the tumour cells completely in the negative cases, or has changed the character of the tumour from a cellular to a more fibrotic type in many of those which still show active growth (*Fig.* 149).

The action of radium on growing cells was well shown in Canti's films of tissue culture, and we may suppose that a similar arrest of their activity occurs when cancer cells come under the influence of radium in the body. But the parts played by the neighbouring connective-tissue cells in phagocytosis of the destroyed cancer cells, and in creating barriers of fibrous tissue around remaining living cells, are processes associated with the action of radium which are difficult to assess but are certainly of great importance in arresting the growth and spread of cancer.

These processes which antagonize the malignant growth—what Sir Anthony Bowlby used to call "holding the cancer cells down"—may even be stimulated

by irradiation, and we must remember that well-stained carcinoma cells do not necessarily indicate actively spreading carcinoma. So long, however, as the epithelial elements appear capable of activity there must be a risk of further spread of the disease if for some reason the "holding down" mechanism were relaxed.

THE BEARINGS OF THE INVESTIGATION UPON THE TREATMENT OF CARCINOMA OF THE BREAST

The final verdict on the value of radium can be given only after consideration of the results obtained in practice—the survival rate of the patients treated thereby. This estimate of the efficacy of radium treatment inevitably introduces a comparison with the results of surgery, and I have therefore plotted out the 3-year and 5-year

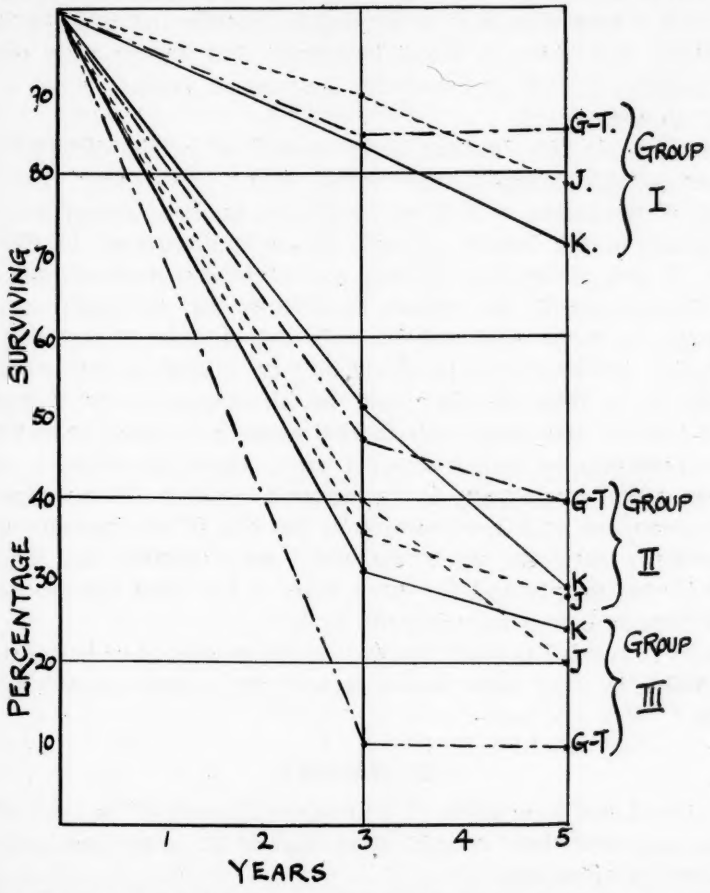

FIG. 155.—Chart showing the 3-year and 5-year survival rates published by Mr. Gordon-Taylor (G-T) and Mr. J. L. Joyce (J) for mastectomy, and by Mr. Geoffrey Keynes (K) for radium treatment for carcinoma of the breast.

survival rates published by Keynes for radium treatment and by Gordon-Taylor and also by Joyce for radical mastectomy without any form of irradiation (*Fig.* 155).

The graph shows that in Group I cases surgery has the advantage over radium—yet it must be remembered even here that the grouping is on a clinical basis in the radium cases and on a histological basis in the cases treated by surgery.

It is certain that the radium 'Group I' includes an unknown proportion of Group II cases, and if the figures could be corrected for this error the radium results would be better than they appear here to be.

In Group II the figures for surgery are much the same as those for radium therapy; but it is a most significant fact that in Group III the survival rate after radium treatment is considerably better than after operation, which must necessarily be an unsatisfactory undertaking in these advanced cases. Figures confirming this superiority of radium in Group III cases have been published elsewhere, and I think it is legitimate to speculate upon the explanation of this phenomenon. Is it possible that bodies derived from cancer cells which have degenerated after irradiation may act as antigens, producing a degree of immunity against carcinoma cells elsewhere in the body? Though this hypothesis has not appeared to have much to support it heretofore, it is interesting to note the statement by Dr. Thomas Lumsden (1937) that there is some indication that cancer cells contain some constituent capable of evoking cytotoxins (anti-cancer bodies) lethal to malignant cells and not to normal cells.

It is a remarkable fact that our experience of the results of radium treatment is better than our histological studies might lead us to expect; and in spite of the presence of carcinoma cells after irradiation in so many of our specimens, persistent disease in the breast or axilla is rarely discovered in the Follow-up Department. Death occurs from visceral and skeletal metastases, and an analysis of 65 cases followed up till the patients died shows that the breast appeared to be free from disease in 50 per cent and the axilla was clear in 75 per cent.

Nevertheless, however good the body may be at dealing with carcinoma cells, we cannot get away from the fact that the histological study of our series has shown active-looking carcinoma cells in the breast in at least 20 per cent of the cases, and it is my opinion that in Group I cases, where the disease is still localized to the breast, radical mastectomy is the wisest treatment. If insertion of radium be the only treatment cells may survive at the site of the primary growth as a possible source for metastatic carcinoma, and I must mention that Keynes himself has recognized this danger and for some years it has been his practice to excise the primary tumour before inserting the radium.

In Groups II and III radium can give results as good as or better than surgery, but it is advisable in these cases also to remove the primary growth whenever this is practicable.

SUMMARY

1. An account has been given of a histological study of 50 cases of carcinoma of the breast examined three months after, and of 22 cases examined six months after, the insertion of radium.

2. Examination of all parts of the breast tissue in the early members of the series failed to reveal any secondary foci of carcinoma in the breast itself.

3. Carcinoma of the breast occurs in several histological types which vary in their sensitivity to radium treatment. There is some evidence that axillary metastases show a similar variation.

4. It follows from this that it is wise to excise the primary tumour as a step in radium treatment, and that radical mastectomy must be the safest treatment for carcinoma in its early stage.

5. The effects of radium upon metastases in the axillary glands are better than is commonly supposed, and experience shows that in all but the early stage of carcinoma of the breast results may be obtained by radium treatment which are as good as, and may be better than, those obtained by radical mastectomy.

My lecture records the work of a team, originally directed by Professor G. E. Gask, and I would like to acknowledge our indebtedness to him; also to the British Empire Cancer Campaign for a grant towards the expenses of the investigation; to Mr. F. H. Aitken Walker and Mr. A. M. Boyd who were the Chief Assistants responsible for keeping the case records and supervising the histological work; and to Miss Margaret Vaughan of the Dunn Laboratories, St. Bartholomew's Hospital, who has done the photography required for the investigation and for this lecture.

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THE DISTRIBUTION AND TREATMENT OF EXTRA-ARTICULAR FOCI IN TUBERCULOUS ARTHRITIS OF THE HIP-JOINT*

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Cases of tuberculous disease of the hip showing bone involvement may be subdivided when seen at an early stage into those which show radiographic evidence of involvement of the joint surfaces and those which show only an extra-articular focus. In this paper only the latter are considered.

I have reviewed 55 cases of extra-articular disease which have been treated in the Country Branch of the Royal National Orthopædic Hospital during the decade 1927–37. The patients were all children, the average age being 5·4 years, the maximum 13 years, and the minimum 9 months.

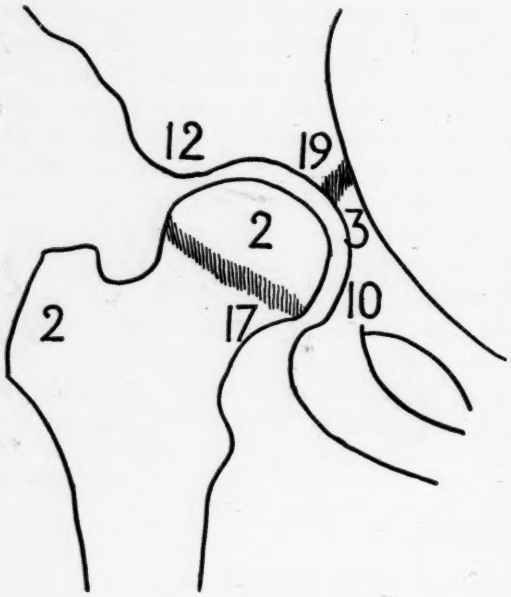


Fig. 156.—Showing frequency of primary foci around hip-joint in the different situations.

The cases are subdivided according to the situation of the lesion or lesions as observed in the earliest radiographs (*Fig.* 156), and it will be seen that the commonest focus was in the medial half of the acetabular roof and the next most common in the femoral neck.

The eradication of an extra-articular tuberculous focus before the neighbouring joint is involved is a procedure which, at any rate in theory, appeals to all undertaking the treatment of cases of bone and joint disease. Of the foci enumerated, it might be considered possible to deal radically with those in the lateral part of the acetabular roof, in the femoral neck, and in the region of the great trochanter; the other regions are more difficult of access.

Of these 55 cases 12 have been treated by excision or curettage of the bony focus, followed by the usual conservative treatment, either on an abduction frame or by traction by means of a weight and pulley; the remaining 43 cases were treated purely conservatively, no attempt having been made to excise the

* A Paper read at the British Orthopædic Association meeting held at Stanmore in May, 1938.

extra-articular focus. In all cases, healing of the lesion has not been considered present until three consecutive radiographs, taken at three-monthly intervals, have shown no further bone destruction and until good definition has become visible in the diseased area.

Of the 43 cases treated purely conservatively, involvement of the hip-joint occurred in 40; in 3 cases only the joint remained free from disease.

Of the 12 cases dealt with by excision of the extra-articular focus followed by conservative treatment, involvement of the hip-joint occurred in 11. In only 1 case did the joint remain free; the lesion was in the region of the great trochanter, from which a large abscess was evacuated.

Thus it is seen that in those cases treated conservatively the joint escaped in only 7 per cent, and in those treated by excision of the extra-articular focus followed by conservative treatment in 8·3 per cent, a difference too small to be significant (*Table I*).

Table I.—SUMMARY OF RESULTS OF TREATMENT

	Cases	
Conservative Treatment :—		
Number in which joint was ultimately involved	40	7 per cent free
Number in which joint remained free	3	
Radical Treatment :—		
Number in which joint was ultimately involved	11	8·3 per cent free
Number in which joint remained free	1	

After excision of an extra-articular focus there was often an interval of considerable improvement both clinically and radiographically, but in spite of a period of conservative treatment the joint was involved in 11 cases out of 12.

EXAMPLES OF JOINT INVOLVEMENT AFTER EXCISION OF A BONY FOCUS

Case A.—P. V., born 1931.

April 25, 1936: Admitted to hospital. Radiograph showed a cavity with sequestrum in the inferior part of the left femoral neck. The joint was normal (*Fig.* 157, A).

May 15, 1936: Curettage of cavity and sequestrectomy through a tunnel in the femoral neck; tubercle bacilli found in material removed.

Operation followed by conservative treatment on abduction frame with traction. Later radiographs show at first healing of the cavity, but that taken on March 18, 1938, shows definite joint involvement (*Fig.* 157, B–D).

Case B.—S. W., born 1931.

Feb. 8, 1935: Admitted to hospital on account of pain in the left hip. Radiograph showed a cavity in the femoral neck, with a normal joint (*Fig.* 158, A).

Feb. 22, 1935: Excision of mass in femoral neck; tubercle bacilli found in material removed. Operation followed by traction by means of weight and pulley.

Dec. 24, 1936: Walking permitted in a patten-ended (i.e., weight-relieving) calliper.

Aug. 6, 1937: Discharged home.

April 22, 1938: Re-admitted to hospital on account of severe pain in the hip.

Radiographs after operation showed progressive healing of the cavity in the femoral neck (*Fig.* 158, B–D); radiograph taken on Sept. 11, 1936, shows an ill-defined cavity in the medial wall of the acetabulum (*Fig.* 158, E). Radiograph on re-admission shows undoubted involvement of the hip-joint (*Fig.* 158, F).

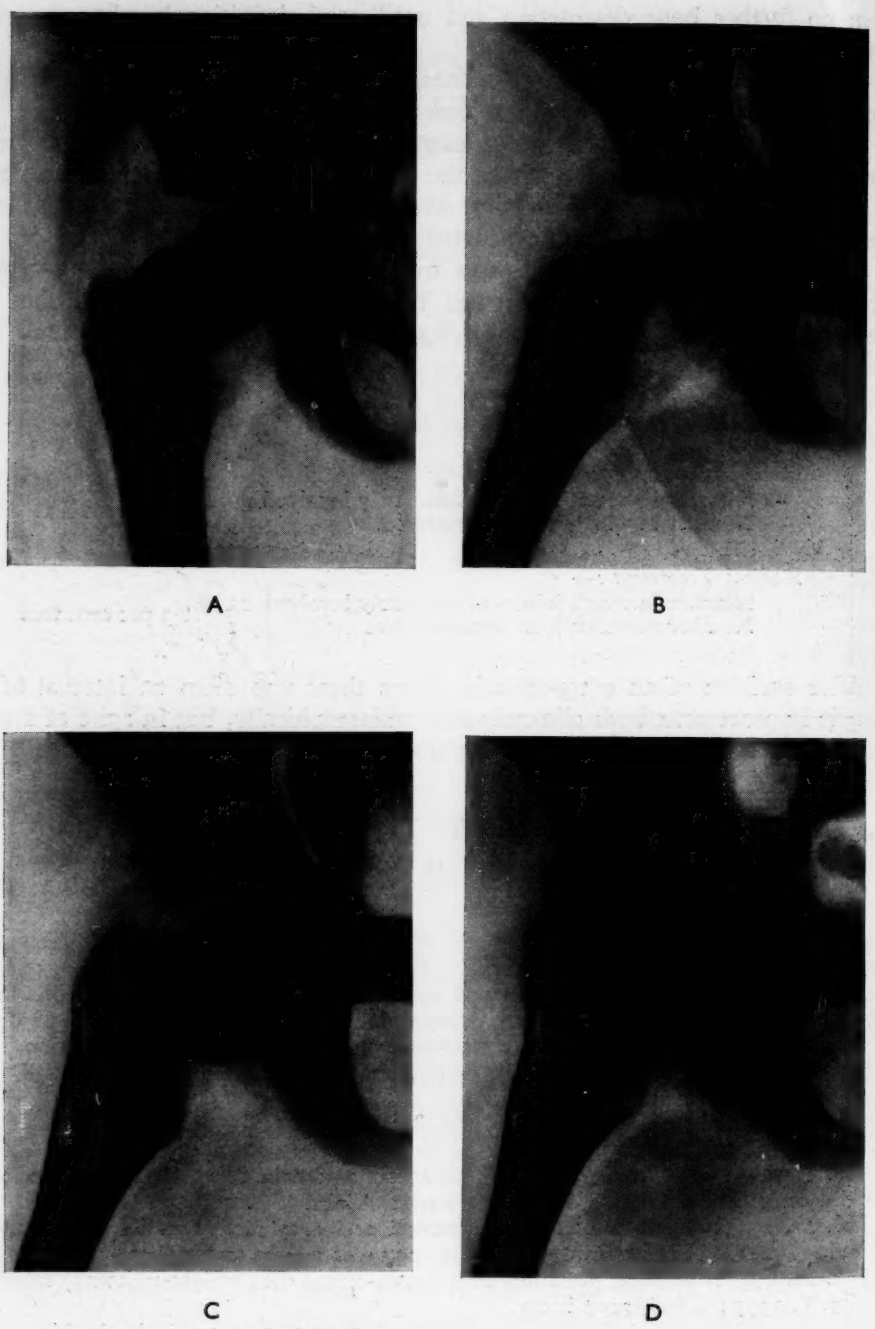


FIG. 157.—*Case A.* A, Showing lesion in inferior part femoral neck on April 27, 1936. B, On June 5, 1936, after curettage of cavity and sequestrectomy. C, On February 22, 1937, showing healing of lesion in femoral neck. D, On March 18, 1938, showing involvement of joint.

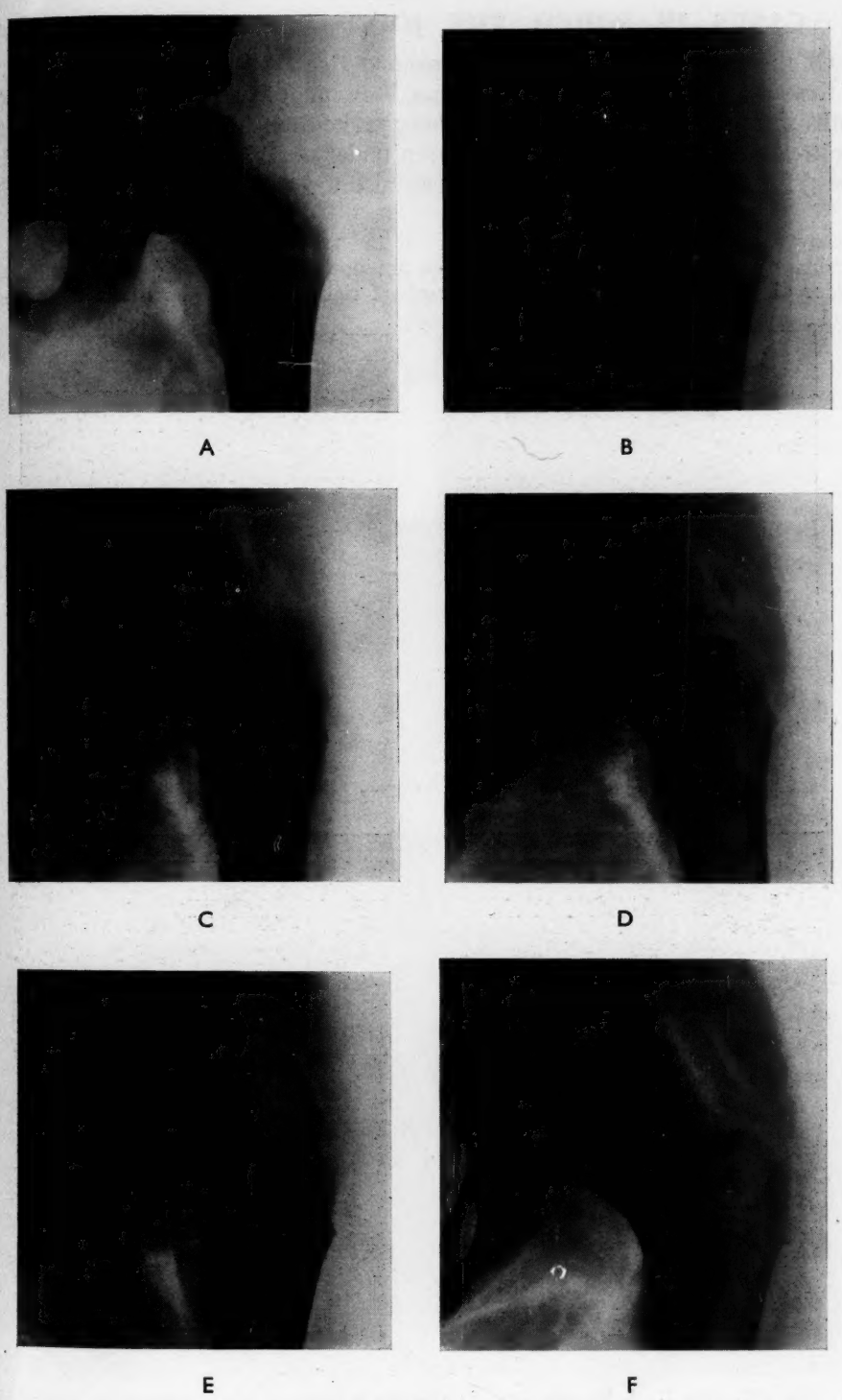


FIG. 158.—*Case B.* A, Showing cavity in inferior part of femoral neck on February 16, 1935. B–D, Showing healing of lesion in femoral neck. E, On September 11, 1936, showing cavity in medial wall of acetabulum. F, On April 25, 1938, showing joint involvement.

CASES IN WHICH THE JOINT REMAINED INTACT

Of the four patients who have remained free from disease in the joint, the one treated by excision of the focus has been under observation for only fifteen months since discharge and the joint cannot yet be considered safe (*Case* 1); of the three treated conservatively two have been under observation for 4 years, and one (*Case* 4) for 10 months, and in this last case also the joint cannot yet be considered safe.*

Case 1.—J. A., born 1932.

Nov. 17, 1933: Admitted to hospital on account of limp; he also had a tuberculous shoulder diagnosed in July, 1933. Radiograph of right hip showed an area of rarefaction

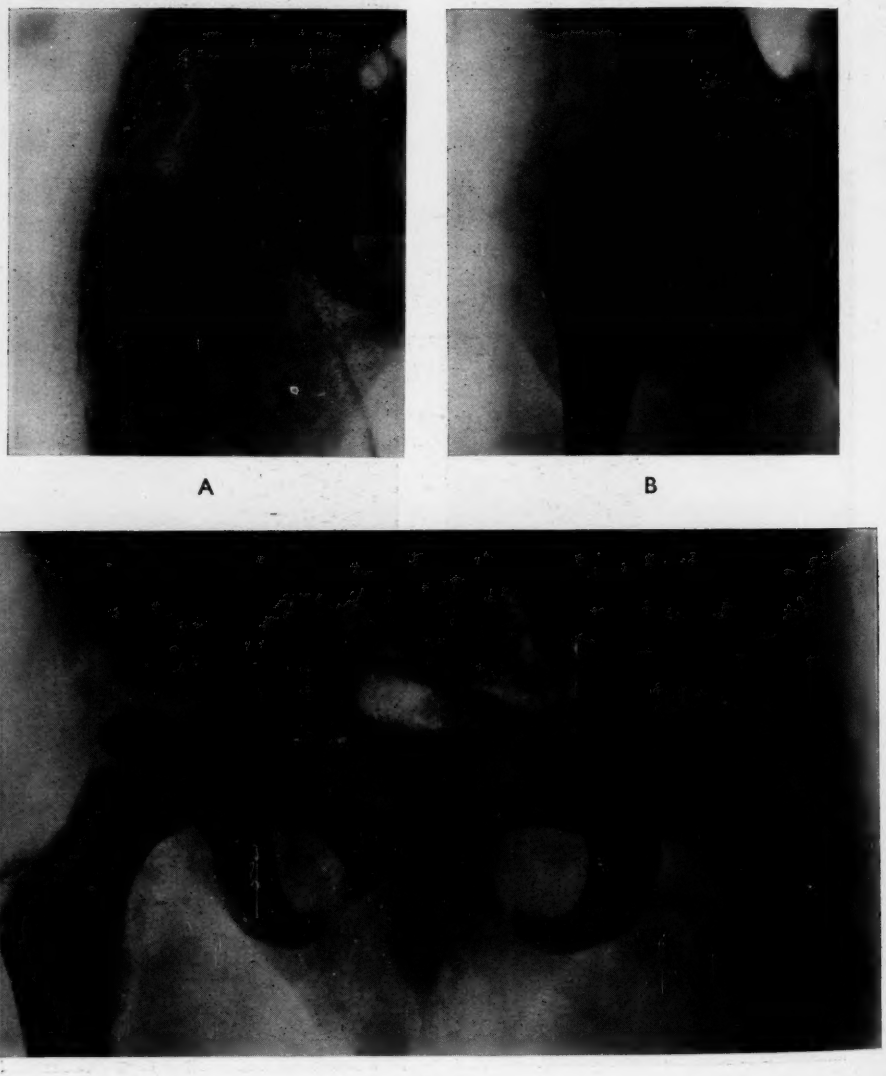


FIG. 159.—*Case* 1. A, Showing area of rarefaction in region of great trochanter on January 22, 1934. B, On December 8, 1934, after evacuation of abscess. C, On November 26, 1937, showing healed lesion.

* *See* footnote on p. 232.

in the region of the great trochanter (*Fig.* 159, A). Later an abscess appeared on the outer side of the thigh.

May 19, 1934: Evacuation of abscess in thigh and in region of great trochanter, followed by treatment on an abduction frame. Radiograph (*Fig.* 159, B).

June 22, 1936: Walking permitted in a patten-ended calliper.

Feb. 20, 1937: Discharged home.

Nov. 26, 1937: Radiograph shows healed lesion in trochanteric region without joint involvement (*Fig.* 159, C).

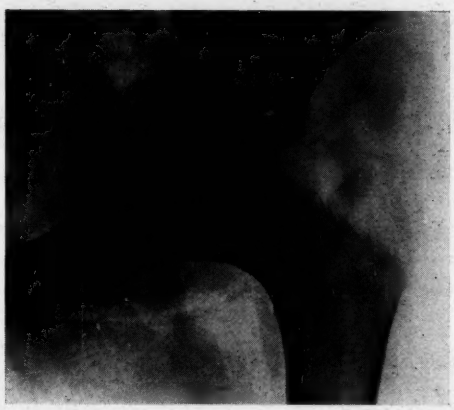
Case 2.—L. C., born 1922.

Feb. 13, 1933: Admitted to hospital on account of limp. Left hip held in position of 15° flexion and 5° adduction; range of movement, flexion 15°–90°, abduction 0°–10°. Radiograph showed considerable cavitation in the ilium; the joint was normal (*Fig.* 160, A). Treated by traction.

Dec. 30, 1933: Walking permitted in patten-ended calliper.

March 9, 1934: Discharged home.

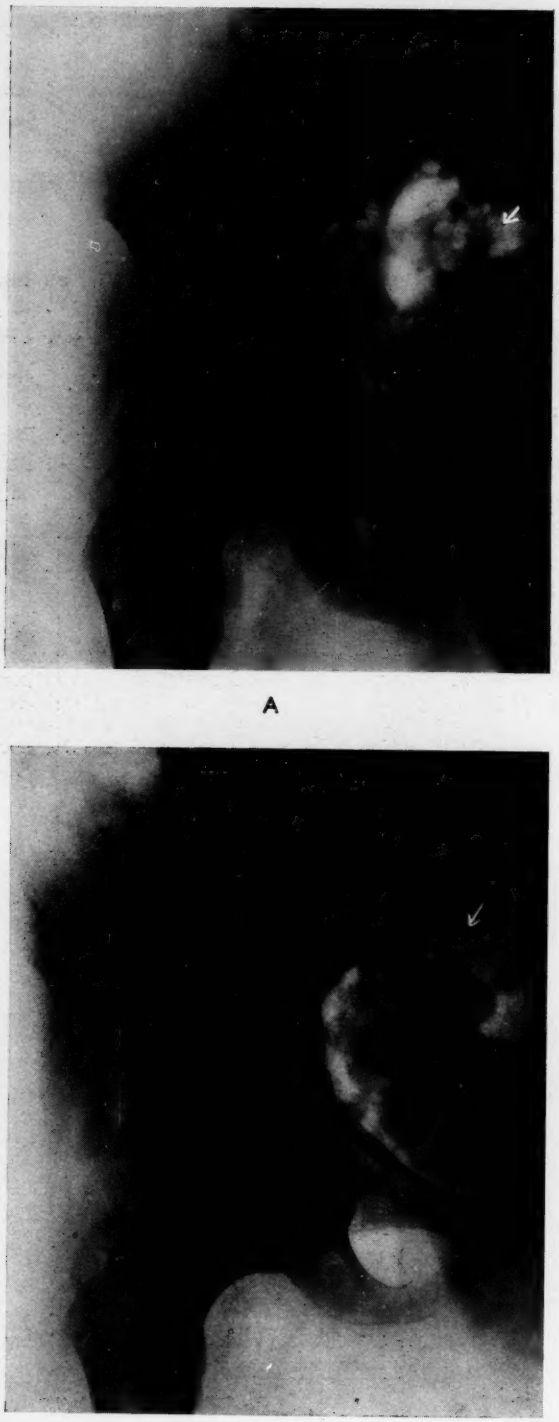
Feb. 11, 1938: Full range of movement present in left hip. Radiograph shows that the cavities in the ilium have disappeared and there is only slight narrowing of the joint space (*Fig.* 160, B).



A

B

FIG. 160.—*Case* 2. A, Showing cavities above acetabular roof on July 12, 1933. B, On October 19, 1936, showing disappearance of cavities in ilium.



A

B

FIG. 161.—*Case* 3. A, Antero-posterior view, showing lesion in medial wall of acetabulum. B, Oblique view, showing more clearly the amount of bone involvement. Arrow indicates edge of intrapelvic abscess.

Case 3.—G. F., born 1924.

Jan. 26, 1932: Admitted to hospital on account of limp. Right hip in position of 75° flexion and 15° abduction; no movement possible on account of muscle spasm. Radiograph showed a lesion in the medial wall of the acetabulum (*Fig.* 161). Treated by traction.

May 31, 1932: Abscess in right iliac fossa. This was aspirated and tubercle bacilli were found in the pus.

Dec. 16, 1933: Walking permitted in patten-ended calliper.

June 1, 1934: Discharged home. Range of movement in right hip almost full.

June 5, 1936: Hip-joint still free.

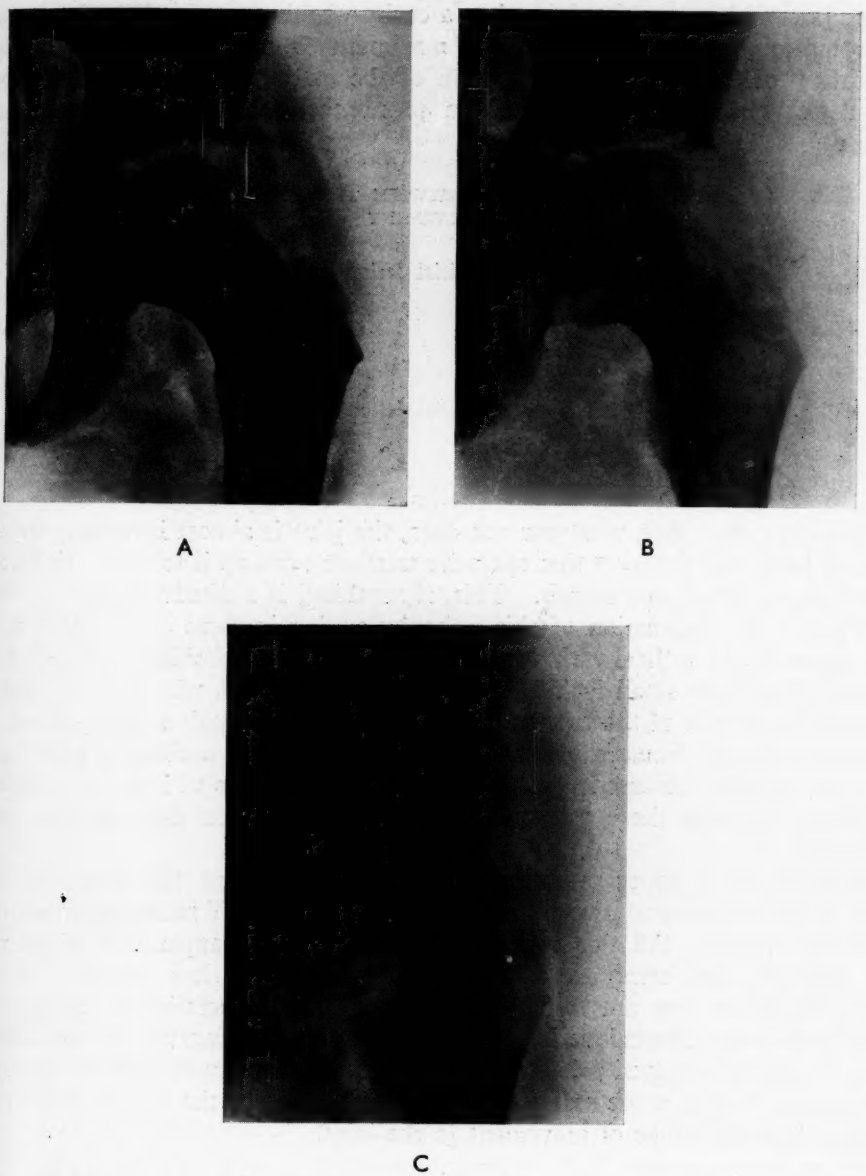


FIG. 162.—*Case* 4. A, Showing lesion in acetabular roof on January 25, 1935. B, On May 28, 1937, showing good definition of lesion with normal joint space and smooth femoral head. C, On November 5, 1938, showing intense rarefaction and involvement of joint.

Case 4.—P. W., born 1929.

Jan. 11, 1935: Admitted to hospital. Range of movement of left hip, flexion 30°–120°, abduction 30°, adduction 10°. Radiograph showed a lesion in the left acetabular roof, but no involvement of the joint (*Fig.* 162, A). Treated by traction.

July 12, 1937: Discharged home walking in patten-ended calliper. Range of movement on discharge: flexion 0°–80°, abduction 40°, adduction 35°, external rotation 10°, internal rotation 0° (*Fig.* 162, B).

March 14, 1938: Range of movement as on discharge.*

Coming now to the remaining 51 cases; of those treated conservatively the average interval between the time when a cavity was first seen and the involvement of the hip-joint was 16·4 months, the maximum 64 months, and the minimum 2 months; of those treated by excision of the extra-articular focus the average interval was 17·6 months, the maximum 42 months, and the minimum 6 months (*Table II*).

Table II.—Time Interval between Treatment and Joint Involvement

Conservative Treatment :—		
Average interval between initial lesion and joint involvement	16·4	months
Maximum interval	64·0	,,
Minimum interval	2·0	,,
Radical Treatment :—		
Average interval between initial lesion and joint involvement	17·6	months
Maximum interval	42·0	,,
Minimum interval	6·0	,,

It is clear then that, whatever one does, the joint is almost invariably involved sooner or later, and the most that operative treatment can do is to delay the invasion of the joint by about one month. This, if anything, is a disadvantage.

What is the explanation of this unhappy ending in these cases which at first sight appear likely to heal with an intact joint? In all probability it is due to the presence of multiple small foci. This is the view of Calvé, who believes that one can never be certain of the extent of the disease, even though a well-defined, and apparently solitary, focus is present. For example, when excising a knee in one case of tuberculous disease in this hospital, we came across at least six cavities in the femur, although there was only one small bone lesion demonstrable radiographically.

Erlacher, in a paper published in 1935, demonstrated that for each focus visible in the antero-posterior view several can be shown if radiographs are taken in different planes. All this renders the excision of an apparently single focus more difficult, and complete eradication of the disease less certain. In fact, Erlacher considers one must often do a very extensive operation in dealing with an extra-articular tuberculous lesion, even removing the capsule of the joint, as this is frequently involved; in spite of this, he considers such extensive operative treatment justified in some cases, as he believes it shortens the length of treatment and gives a useful range of movement in the joint.

* Since writing this paper I have seen the patient P. W. (*Case* 4), of those reported as recovering with an intact joint. He now has definite evidence, both clinical and radiological, of involvement of the hip-joint. The radiograph is shown in *Fig.* 162, C.

SUMMARY

1. In extra-articular tuberculous disease of the hip the gain obtained by excision of the obvious focus over pure conservative treatment is too small to be of significance.

2. After excision of the obvious focus, local as well as general improvement often occurs, leading to a false sense of security.

3. Involvement of the joint may occur after as long an interval as two years, however efficient the treatment.

4. Less than 10 per cent of children with extra-articular tuberculous disease of the hip recover with an intact hip-joint.

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THE CAUSES OF RELAPSE FOLLOWING SYMPATHECTOMY OF THE ARM*

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THE disappointing results of sympathectomy in the treatment of vascular disease of the hands are still incompletely explained. They have proved to be the experience of all surgeons working in this field of vascular disease (Adson and Brown, 1929; Telford, 1932, 1934; Livingston, 1935; Gask and Ross, 1937), and it is the more surprising because of the permanent success of lumbar ganglionectomy in the treatment of similar conditions in the feet. Recurrence of symptoms

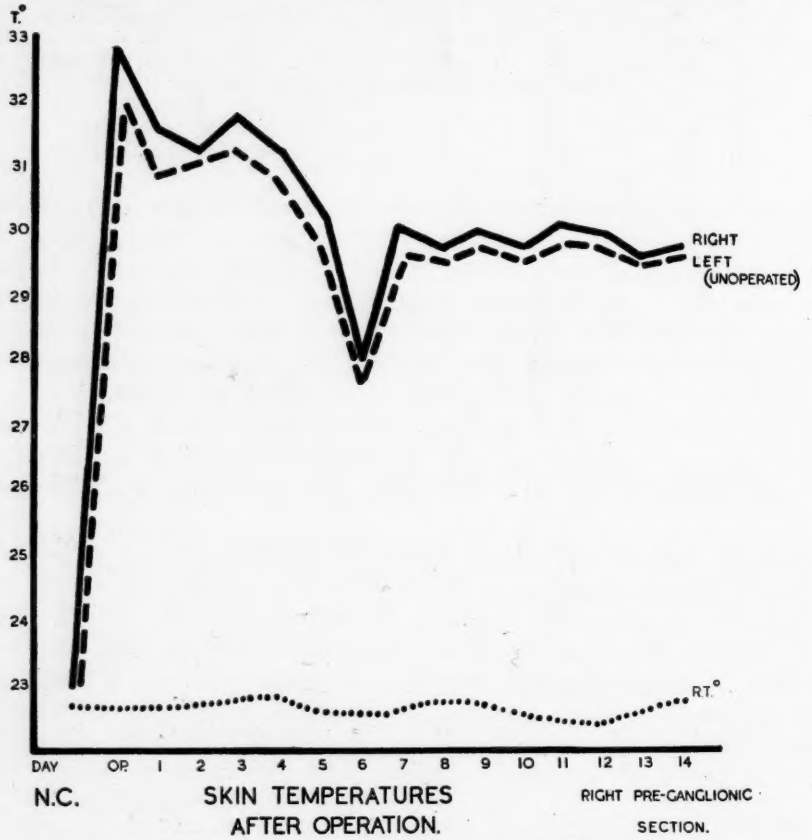

FIG. 163.—Chart of post-operative arm temperatures immediately after operation.

* From the Department of Clinical Research in Disorders of the Autonomic Nervous System, Royal Infirmary, Manchester.

frequently follows sympathectomy of the arm, and the search for the cause of this relapse is one of the largest problems to-day in vascular surgery.

Since 1932 this problem has been a subject of special inquiry in Professor Telford's clinic, and we have had as material for research 38 cervicothoracic ganglionectomies done between the years 1931–34 and 29 ' preganglionic ' sections of the thoracic cord performed since February, 1935. Constant review of these cases has revealed the frequent reappearance of symptoms in the hands, and has at the same time emphasized the necessity for a clear definition of relapse.

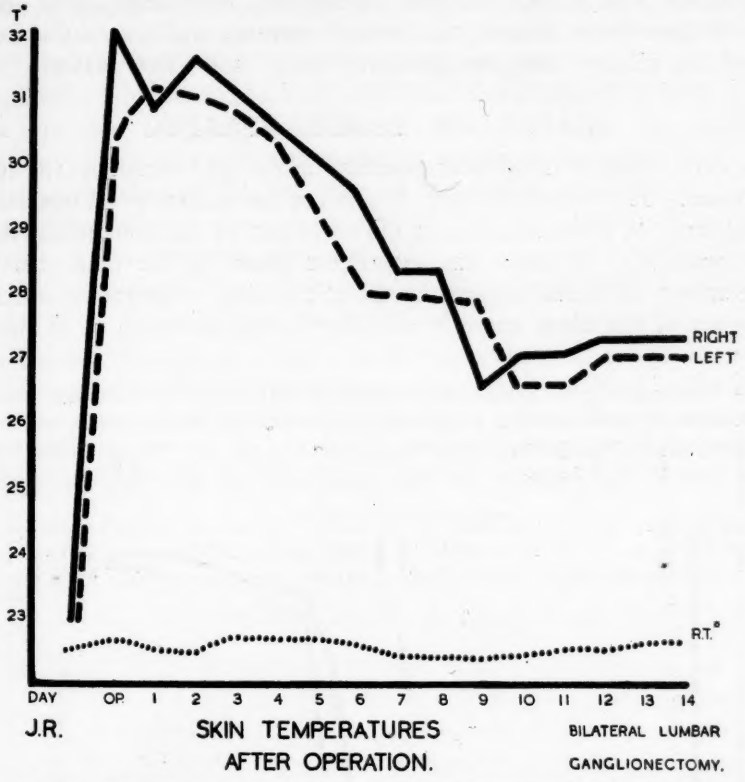

FIG. 164.—Chart of post-operative feet temperatures immediately after operation.

Immediately after sympathetic denervation, of whatever nature, there is always an improvement in the condition of the fingers except where actual digital thrombosis or extreme sclerodactyly exists. The high skin temperature resulting from the operation is not, however, maintained, and a steady decline occurs until a level is reached which is usually several degrees above the pre-operative temperature. This decline of the skin temperature after sympathectomy occurs both in the hands and in the feet (*Figs.* 163, 164), and appears even when the operation is performed for non-vascular disease. It is a normal sequel to all types of sympathectomy operations, and is presumably due to the resumption of a certain degree of tone by the blood-vessels by virtue of their inherent muscular activity. The sudden drop in the temperature which occurs about the sixth day may indicate an acceleration of this process by the onset of hypersensitivity of the blood-vessels to circulating adrenaline, as shown by White. Smooth muscle deprived of its sympathetic

nerve-supply shows this hypersensitivity when degeneration of the nerves is complete, but sensitization cannot be the sole cause of the fall in skin temperature after operation, for a considerable decline has already taken place before the sympathetic nerves have degenerated, and there is no corresponding rise when the hypersensitivity disappears, as we have shown that it does, some months later.

We have not regarded this decline in skin temperature as a relapse after sympathectomy because it is an inevitable sequel, and the value of the operation lies in the residual permanent dilatation of the blood-vessels. We have been concerned rather with clinical relapse. Symptoms have reappeared shortly after operation, or have been delayed for several months, and this difference in time has resolved the relapses into two groups—'early' and 'late' cases.

CASES OF EARLY RELAPSE

In the early relapses it has been essential first of all to examine the adequacy of the denervation. The incompleteness of some of the earlier operations was detected by the persistence of reflex sweating in the hand and by the demonstration, immediately after operation, of intact vasoconstrictor fibres in the ulnar nerve. These fibres were shown to be still present by the rise in skin temperature which followed anæsthetization of the ulnar nerve at the elbow with novocain, as in the following case:—

Case 1.—**Unilateral pre-ganglionic section of the thoracic cord for acrocyanosis. Subsequent history and testing suggesting incomplete denervation.—**

C. Z., aged 26, a greengrocer's assistant, stated that for ten years she had suffered from coldness and blueness of the hands. In the winter months, in spite of wearing gloves, she had

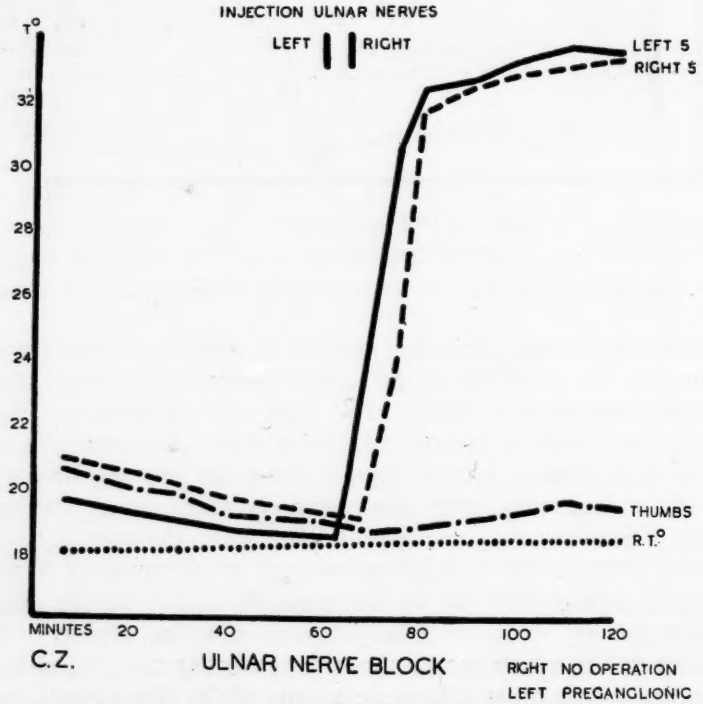

FIG. 165.—*Case* 1. Chart of nerve-block of a case of incomplete denervation showing the similarity in the vasodilatation obtained after operation in the operated and unoperated hands.

severe chilblains, the skin on the dorsum of all the fingers, and even the thumb, becoming fissured and septic. There had never been any white spasm.

ON EXAMINATION.—The fingers and dorsum of the hands were cold and blue, the condition being intensified by immersion in water at 15° without showing, however, any white spasm. There was no sclerodactyly, but many scars of old chilblains and fissures. Pre-operative ulnar nerve-block raised the temperature of the fifth left finger from 20·2° C. to 30·2° C. in fifteen minutes.

OPERATION (May 21, 1935).—By an anterior approach the left thoracic cord was exposed with difficulty owing to numerous large and dilated veins. It was believed to have been crushed and divided below D.2 ganglion, with severance of the rami leading to that ganglion.

SUBSEQUENT PROGRESS.—The day after operation the hand was still bluish on the dorsum, the skin was clammy, and the temperature raised only 4° C. Testing by anæsthetization of the ulnar nerves gave an identical response on both the operated and unoperated sides in the vasodilatation produced in the ulnar area of the hands (*Fig.* 165).

Comment.—This case cannot be considered a true relapse because sympathetic denervation was not completely performed. Four hands in the ganglionectomy series, all done by the more difficult posterior approach, and one of the early pre-ganglionic sections, showed this evidence of incomplete denervation. In some of the early ganglionectomies the importance of the contribution from the second thoracic ganglion had not been realized and the excision was not extensive enough. The *only* preganglionic section which has proved to be incomplete was one of the first cases in which the operation was attempted.

The remaining cases of early relapse, with reappearance of symptoms within a few days of operation, have shown an absence of vasoconstrictor fibres in the ulnar nerve when tested by anæsthetization of this nerve at the elbow, and the median nerve at the wrist. Nine hands after ganglionectomy, and four after preganglionic section, gave this early relapse, and the following are two typical cases in this series :—

Case 2.—**Long history of the Raynaud phenomenon without nutritional changes. Bilateral preganglionic section of the thoracic cords with recurrence of white spasm in the left hand 11 days, and in the right hand 4 days, after operation.**

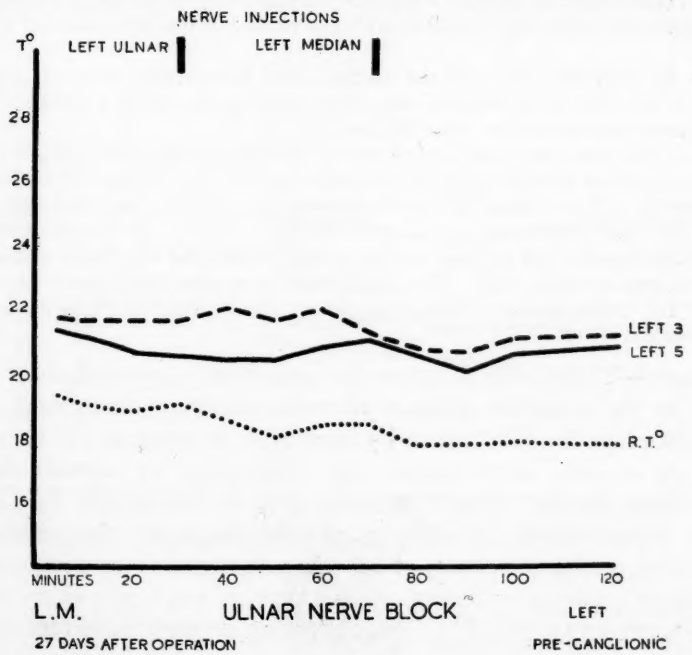

FIG. 166.—*Case* 2. Chart of nerve-block where clinical relapse occurred 11 days after operation but vasoconstrictor fibres are shown to be absent in the ulnar and median nerves.

L. M., housewife, aged 35, with 16 years' history of the Raynaud phenomenon affecting the hands up to the wrist, but not the feet. White spasm lasting many hours, brought on by cold, but not by emotion. Latterly the attacks have been almost as frequent in the summer as in the winter months. No trophic changes.

FIRST OPERATION (October 12, 1937).—Preganglionic section left thoracic cord below D.3 ganglion. Upper end sutured to scalenus anticus.

PROGRESS.—Next day result excellent. The temperature of the hand was 31·4° C. in the ward. No Horner.

October 23, that is, 11 days after operation, white spasm of all fingers up to proximal interphalangeal joints, but painless, and the thumb and the dorsum of the hand were not involved.

SECOND OPERATION (November 2, 1937).—A similar operation upon the right thoracic cord.

PROGRESS.—Next day the temperature of the hand was 33·8° C. in the ward. No Horner.

November 6, that is, 4 days after operation and whilst the patient was still in bed, an attack of white spasm in the right hand. Anæsthetization of the ulnar and median nerves did not reveal the presence of any intact vasoconstrictor nerve-fibres (*Fig.* 166).

The following case was tested over a period of six months :—

Case 3.—**A long history of the Raynaud phenomenon with early sclerosis. A right cervicothoracic ganglionectomy and a left preganglionic section were performed at the same time. Early relapse with no evidence of vasoconstrictor nerves.**

S. A., a cotton spinner, aged 23. Seven years' history of the Raynaud phenomenon in the hands and for the last two years also in the feet. Latterly the attacks have been present in summer as well as during the winter and the pain severe. The fingers crack and ulcerate during the cold weather. She has noticed a little tightness in the skin of the fingers and around the mouth.

ON EXAMINATION.—The fingers and toes show the typical Raynaud sequence of colour changes. The skin is glossy and shows numerous scars of healed ulcers. The skin round the mouth and nose is a little tight and the patient has a pinched look. There are evidently early nutritional changes in the skin.

OPERATION (December 8, 1936).—*Right side* : By an anterior approach the stellate ganglion was widely exposed and removed, together with the second dorsal ganglion and the intervening cord.

Left side : By a similar approach the thoracic cord was divided below D.3 ganglion. All the rami of D.3 ganglion were divided and those running to the D.2 ganglion. The upper cut end of the cord was sutured to the scalenus anticus.

PROGRESS.—The next day there was a severe Horner on the right side, but none on the left, and the temperature of both hands in the ward was 32° C. The daily testing of the limbs in the ward showed rather a rapid decline in temperature, and on her discharge, 14 days after operation, the left hand registered 27° C. and the right 25° C. On arrival home she noticed blueness of all the fingers, but no pain and no white spasm, and they have remained well, but subject to these attacks when cold. The right hand is always worse than the left.

Testing of the limbs has not revealed any intact vasoconstrictor fibres in the ulnar nerves (*Fig.* 167, A and B).

Comment.—These cases illustrate the immediate reappearance of the Raynaud phenomenon in the complete absence of vasoconstrictor fibres, and white spasm was easily induced in the fifth fingers by immersion in water at 15° C., even though, in addition, all somatic nerve-supply was interrupted by anæsthetization of the median and ulnar nerves. There must be here, as postulated by Lewis, a local lesion of the digital vessels of sufficient severity to render the vessels capable of spasm even after complete section of all the preganglionic or postganglionic vasoconstrictor fibres. Objective testing of this type of early relapse by immersion of the hands in water at 15° to 18° C. has shown up an early recurrence of symptoms

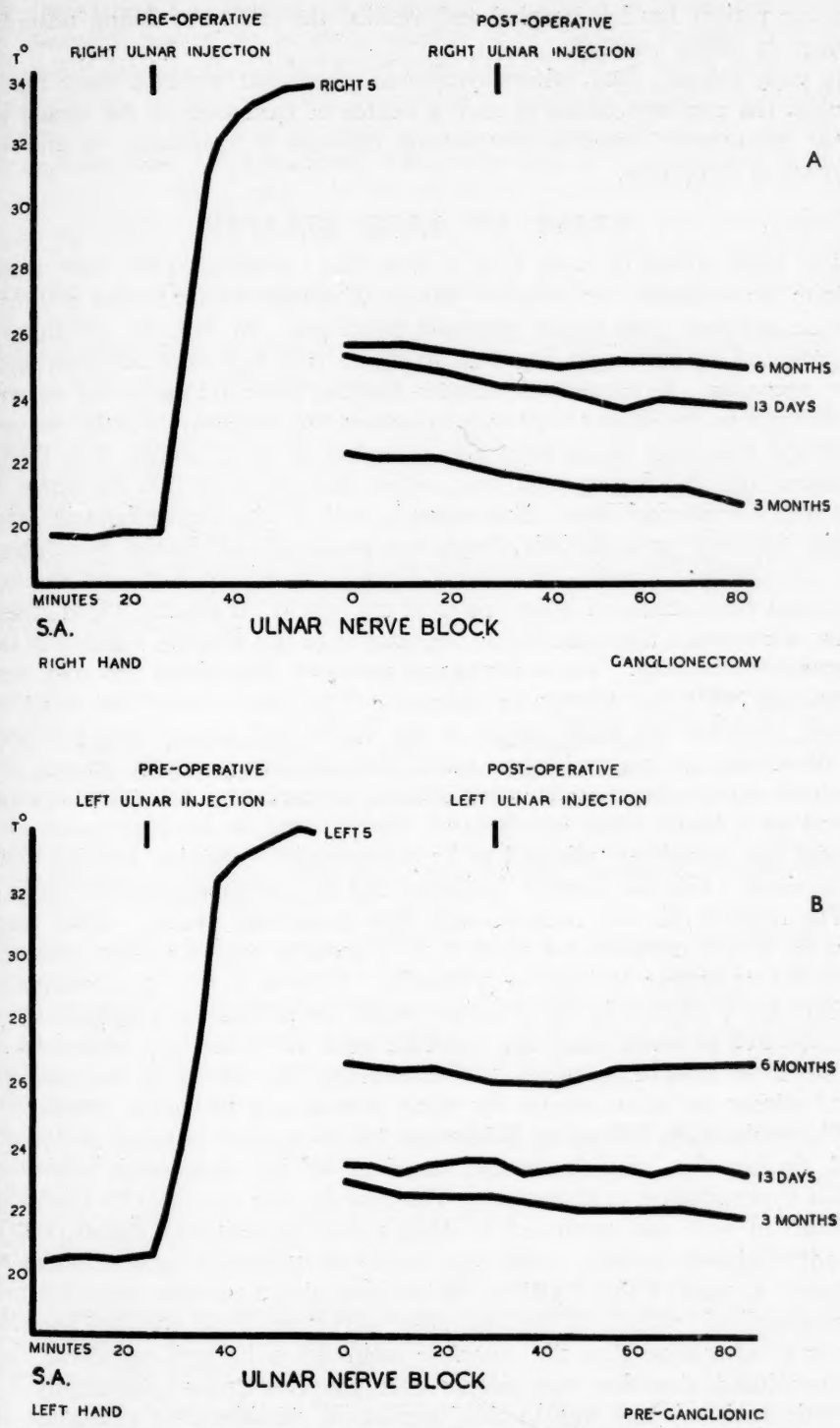

FIG. 167.—*Case* 3. Chart of nerve-block. A, Ganglionectomy right hand; B, Preganglionic section left hand. Clinical relapse 14 days after operation but anæsthetization does not reveal the presence of vasoconstrictor fibres in the ulnar nerve of either hand over a period of 6 months.

before the patient has left hospital and avoided the fallacy of dating relapse from the onset of cooler weather.

In early relapse, then, where symptoms reappeared within a short time after operation, the explanation lies in such a degree of local fault in the digital vessels that the presumably complete sympathetic paralysis is insufficient to prevent the recurrence of symptoms.

CASES OF LATE RELAPSE

The larger group of cases have shown 'late' relapse. They have presented a definite improvement, or complete absence of symptoms, for several months after operation and have then begun gradually to relapse. At first the symptoms were only produced by prolonged exposure to severe cold and were never so severe as before operation. Gradually the attacks became more frequent and severe and were brought on by shorter exposures to milder temperatures. Finally the patients complained that their hands were almost as bad as ever, though they frequently volunteered that the fingers went blue, rather than white, or that the extent of the white spasm was much less. For example, one of the cervicothoracic ganglionectomies operated upon in July, 1933, was perfectly well in the November, but when seen the next January stated that during a recent spell of cold weather she had noticed brief attacks of white spasm at the tips of her fingers, which afterwards became bright red. She attached no importance to this finding, which was elicited by careful questioning. These symptoms persisted throughout the cold weather, disappearing with the advent of summer. The next winter the white spasm recurred, affecting the whole length of the fingers and lasting twenty minutes or so. Afterwards the fingers became bright red and then gradually became normal. The third winter the thumbs were affected as well and the white spasm was followed by a bluish-black discoloration which lasted an hour or more. In fact the hand had completely relapsed to its pre-operative condition and has remained so ever since. Also the Horner syndrome had to a large extent recovered.

The time of this late relapse varies from patient to patient. After ganglionectomy it is not manifest for from 6 to 9 months, whereas after preganglionic section it may appear as early as 3 months. Relapse is not an invariable sequel and there are 3 patients in the clinic on whom cervicothoracic ganglionectomy was performed five to seven years ago and who have never had any symptoms in the hand since the date of operation. In considering any theory of the cause of this type of relapse we must account for these permanently successful results.

The explanation offered by White and his co-workers is based on the physiological finding that smooth muscle, deprived of its sympathetic nerve-supply, becomes hypersensitive to adrenaline. This reaction was described by Lewandowsky in animals in 1903 and confirmed by Meltzer and Auer (1904), Elliott (1905), and Dale and Richards (1918). Lewis and Landis in 1930 first drew attention to the occurrence in man of this reaction. White and his co-workers were able to show that preganglionic section of the vasomotor nerves rendered the blood-vessels less sensitive to adrenaline than did complete denervation by post-ganglionic excision. They concluded, therefore, that relapse after ganglionectomy (presumably a post-ganglionic excision) was due to this increase in sensitivity to adrenaline of the smooth muscle of the vessel walls, and advocated preganglionic section of the vasomotor nerves.

The realization that lumbar ganglionectomy is largely a preganglionic section of the vasomotor nerves of the foot, whereas cervicothoracic ganglionectomy is a postganglionic excision for those of the arm, led Telford, in 1935, to modify the technique of the cervical operation by making a preganglionic section, cutting the cord below the third thoracic ganglion and dividing the rami of the second and third thoracic nerves. Independently, Livingston (1935) advocated and performed a similar operation, but pointed out the difficulty, owing to the lack of knowledge of the postganglionic cell stations for the arm, of interpreting the better results he obtained from this operation. The preganglionic operation has now displaced ganglionectomy for the arm and White's hypothesis is being offered as the explanation of relapse.

We have investigated this hypothesis, using the intravenous adrenaline test devised by Freeman, Smithwick, and White (1934):—

Normal saline is run into the median basilic vein at the rate of 40 to 60 drops per minute. After half an hour an adrenaline solution of 1 in 250,000 saline is substituted, the patient being unaware of the change. The transfusion is continued for a period of a half to one hour and skin temperature and pulse readings are taken at five-minute intervals. Except for slight headache and some palpitation, no unpleasant symptoms are experienced. There is always striking pallor of the face, especially in the circumoral region, and to a lesser degree in the hands and fingers, which appears shortly after the adrenaline has been started and persists until a few minutes after the adrenaline has been stopped. The pallor in the face is not accompanied by any appreciable drop in skin temperature, indicating that the effect is mainly upon the minute vessels. In the fingers and hands the skin temperature decreases if it is above that of the room and the arterioles are sensitive to the adrenaline. The hands were kept under the bedclothes so that they were in a warm and constant atmosphere throughout the experiment. When the adrenaline is stopped there is profuse blushing of the face within 3 to 4 minutes, followed in 5 to 10 minutes by a similar flushing of the hands. With the reddening of the hands there is a rapid rise in the skin temperature up to that of full vasodilatation. This reaction appears to be similar in many ways to the 'overswing' occurring in response to cold, described by Lewis (1930). In some of our earlier cases where the temperature of the fingers was initially low—i.e., about room temperature—no further drop could occur, yet when the adrenaline was stopped a rapid 'overswing' up to a high temperature occurred, indicating release from a vasoconstrictor effect of the adrenaline.

We have confirmed the observation of Smithwick, Freeman, and White (1934), corroborated in animal experiments by Grant (1935) and Ascroft (1937), that following preganglionic section the hypersensitivity of the blood-vessels to adrenaline is less than after postganglionic excision, but we have found that after both types of operation this hypersensitivity has decreased with time. The following two cases illustrate these points:—

Case 4.—E. P., a dressmaker, aged 23, with ten years' history of the Raynaud phenomenon, but no nutritional changes in the fingers.

OPERATION (January 19, 1937).—

Right side: Preganglionic section of thoracic cord below D.2 ganglion.

Left side: Cervicothoracic ganglionectomy.

PROGRESS.—Regular testing with intravenous adrenaline showed less hypersensitivity on the side of the preganglionic operation and its more rapid disappearance. After six months the hypersensitivity was hardly detectable and at twelve months it had disappeared, yet both hands were equally warm and satisfactory. After fifteen months the hand on the side of the preganglionic section became progressively cooler, and when examined eighteen months after operation the hypersensitivity to adrenaline had disappeared, but for the first time it was possible to produce white and blue spasm in the fingers by immersion of the hand in water at 15° C. The decrease in hypersensitivity is shown in *Figs.* 168 A and B, and the ganglionectomy (*Fig.* 168, B) shows greater and more lasting sensitivity than the preganglionic section (*Fig.* 168, A).

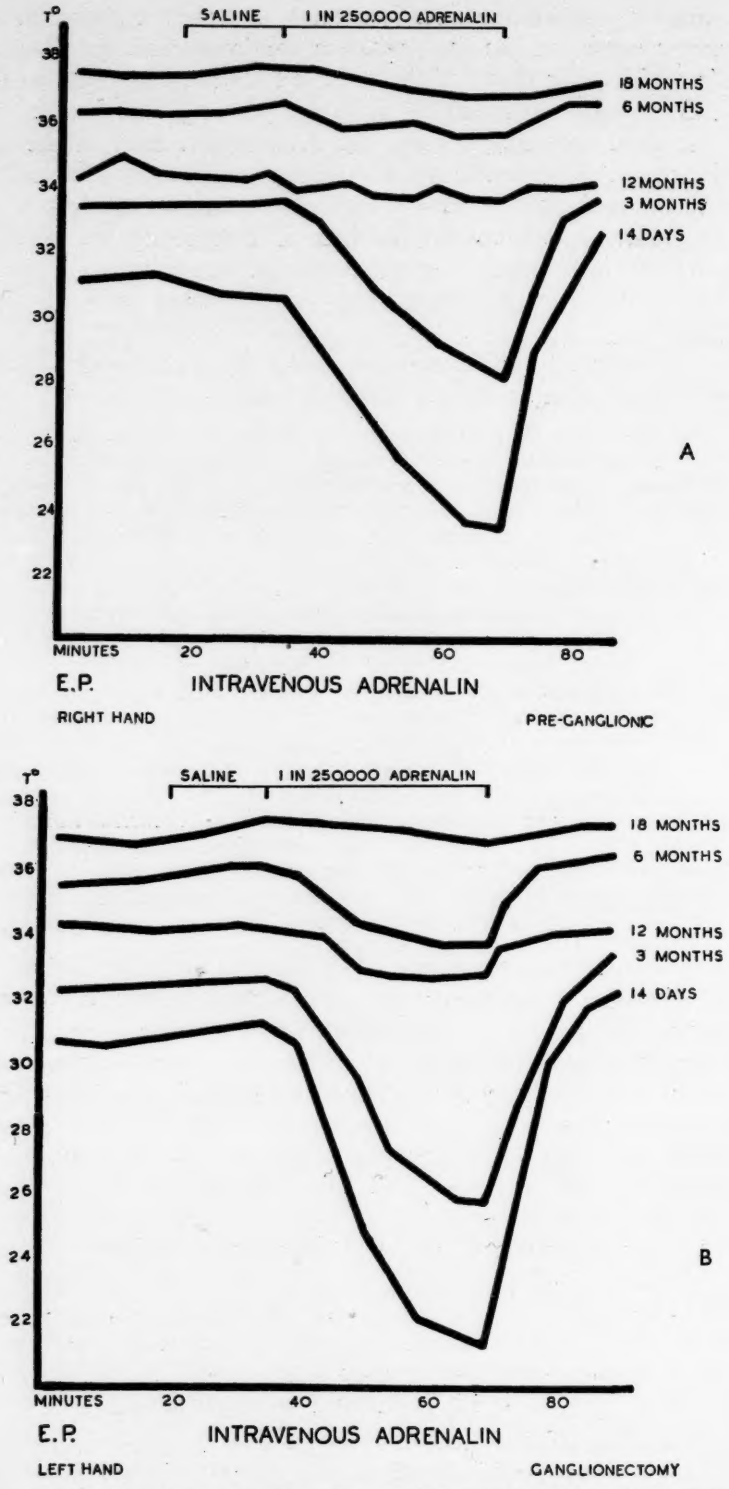

FIG. 168.—*Case* 4. Intravenous adrenaline. The sensitivity to adrenaline gradually decreases with time but persists longer and is more pronounced after the ganglionectomy operation.

Case 5.—M. E., a greengrocer's assistant, aged 22, with seven years' history of the Raynaud phenomenon, but no nutritional changes in the fingers.

OPERATION (December 15, 1936).—Left preganglionic section below D.2 ganglion. This patient was not very sensitive to the intravenous adrenaline and strengths of 1–125,000 and 1–62,500 were used in addition to the 1–250,000 on each visit. The hypersensitivity had practically disappeared at 11 months, but up to the present time there is no evidence of relapse. The chart of her tests is shown in *Fig.* 169.

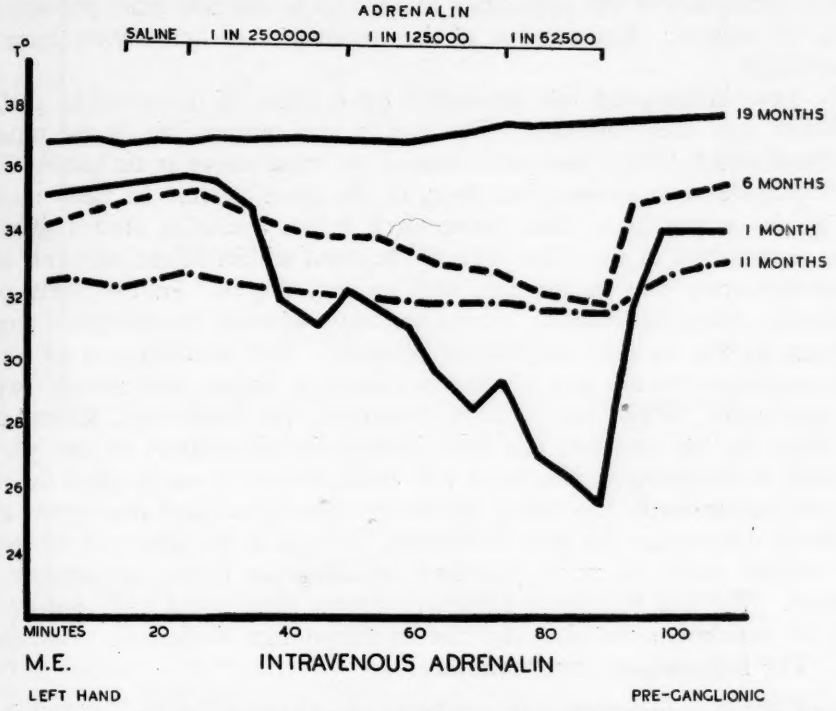

FIG. 169.—*Case* 5. Intravenous adrenaline, showing the decrease in sensitivity over a period of 19 months though no clinical relapse occurred.

It is evident that this hypersensitivity of the blood-vessels to adrenaline is at its greatest when it first appears, 8 to 10 days after operation, and that it steadily decreases, being always less at the time when these late clinical relapses occur.

For the following reasons we have been unable to accept White's explanation of the cause of relapse :—

1. Hypersensitivity appears at its maximum from 8 to 10 days after operation, whereas the usual clinical relapses are not evident for several months.

2. At the time when relapse is becoming apparent the hypersensitivity to adrenaline is either non-existent or very much diminished and continually decreasing, whereas the relapse is steadily becoming worse.

3. The preganglionic sections which have relapsed have done so sooner than corresponding ganglionectomies (compare *Case* 4, quoted above), yet the sensitivity is greater after ganglionectomy than preganglionic section.

4. The occasional permanently successful result following ganglionectomy is unexplained by this hypothesis.

5. Lewis (1938) has pointed out that if recurrence of symptoms is due to a new factor of compensation, such as hypersensitivity to circulating adrenaline, the

attacks of Raynaud's phenomenon should occur equally after sympathectomy, whether the patients operated upon originally had the Raynaud phenomenon or not. This certainly does not occur. We have carefully observed two young patients in Professor Telford's clinic who were operated upon a year ago for hyperhidrosis of the hands, and there has been no suggestion of the Raynaud phenomenon since their operations.

The inadequacy of this hypothesis compels us to examine other possible causes for this late relapse. Regeneration of the vasoconstrictor nerve-fibres must firstly be considered.

We have investigated this possibility by a series of nerve-blocks performed both before and after operation. The rise in skin temperature in the ulnar area of the hand which follows anæsthetization of the ulnar nerve at the elbow, is proof of the existence of vasoconstrictor fibres in the ulnar nerve. In cases uncomplicated by any scleroderma, ulnar nerve-block before operation always gave a rise in skin temperature of the ulnar area of the hand within fifteen minutes, without any accompanying rise in the 1st, 2nd, or 3rd fingers. In the same patient, immediately following *complete* sympathectomy, whether postganglionic or preganglionic, no rise in skin temperature occurred. The possibility of an accessory median supply to the 4th and 5th fingers (Simpson, Brown, and Adson, 1931) has been considered. White has recently supported this suggestion, stating that in cases where he has obtained but little increase in temperature of the 5th finger after ulnar nerve-block, he has found full vasodilatation to occur when the median nerve was subsequently injected at the wrist. We have found that *after* complete sympathetic denervation has been performed, injection of the ulnar and subsequently of the median nerve has never produced any alteration in the temperature of the 5th finger. We feel that these negative findings after ulnar and median nerve-blocks are conclusive evidence that the operation has divided all vasoconstrictor fibres. The following are two examples :—

Case 6.—S. R., a housewife, aged 44, with six years' history of the Raynaud phenomenon affecting the hands, feet, and nose. She had suffered severely from chilblains in the hands, and on examination there was evidence of very early sclerodactyly in the fingers.

Preganglionic section of the left thoracic cord below D.2 ganglion. Upper end sutured to scalenus anticus. The absence of response in the ulnar area of her left hand to ulnar and median nerve-block, three months after operation, is shown in *Fig.* 170.

Case 7.—L. W., a weaver, aged 40, with five years' history of the Raynaud phenomenon in the hands, sufficiently severe to stop her from working, but with no evidence of sclerodactyly.

Preganglionic section of the left thoracic cord below D.3 ganglion, with division of all branches to D.3 and those rami running to D.2. The upper cut end was sutured to the scalenus anticus.

Fig. 171 shows the absence of vasodilatation in the ulnar area of her left hand which followed anæsthetization of the left ulnar nerve at the elbow and the median nerve at the wrist.

In the course of our investigations two patients who attended regularly for testing after operation showed, after some months, a rise in skin temperature after nerve-block which increased with each subsequent test. Shortly after this detection of vasoconstrictor fibres in the ulnar nerve, the first signs of relapse were noticed, and in the succeeding months the symptoms became steadily worse. The first of these two cases was as follows :—

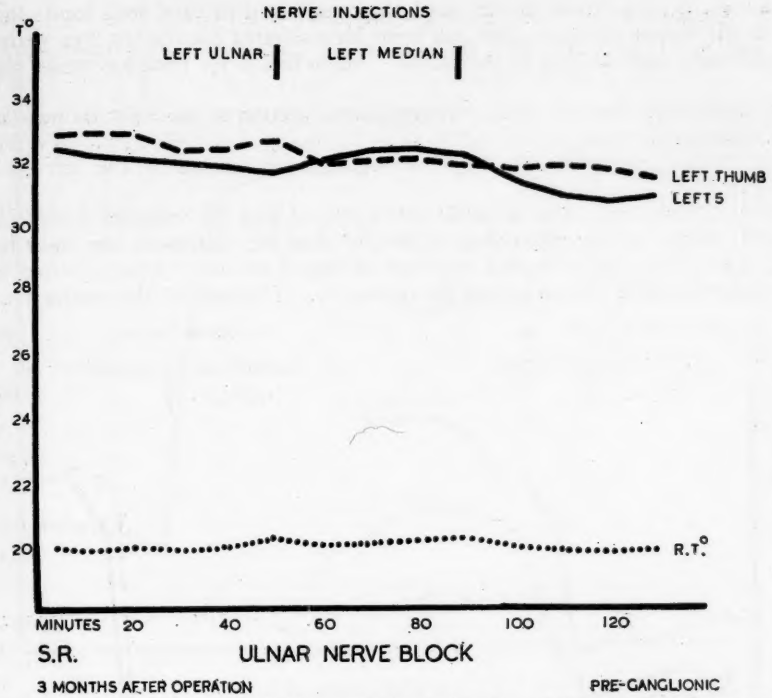

FIG. 170.—*Case* 6. Ulnar and median nerve-block proving the complete absence of vasocorstrictor fibres supplying the hand 3 months after operation.

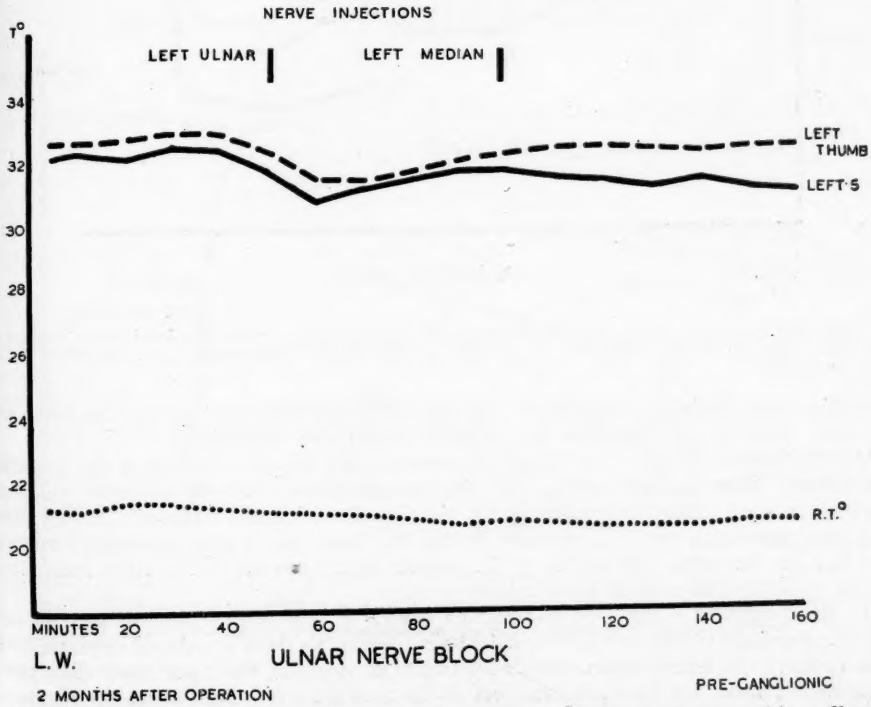

FIG. 171.—*Case* 7. Ulnar and median nerve-block showing the absence of vasoconstrictor fibres supplying the hand 2 months after operation.

Case 8.—A. C., a garment cutter, aged 19, complained of blue cold hands for 12 years, especially in the winter months. She had been incapacitated for the last two years by severe ulcerated chilblains and swelling of the hands. There had never been any white spasm of the fingers.

FIRST OPERATION (June 5, 1936).—Preganglionic section of the right thoracic cord at the level of D.3 ganglion.

SECOND OPERATION (June 18, 1936).—Preganglionic section of the left thoracic cord below D.2 ganglion.

PROGRESS.—The result in both hands was excellent and she resumed work. At the end of September, 1936, slightly more than 3 months after her operation, the right hand began to cool and she noticed that it became blue and swollen if she was worried, excited, or exposed to cold, in just the same way as before the operation. Throughout the winter the condition

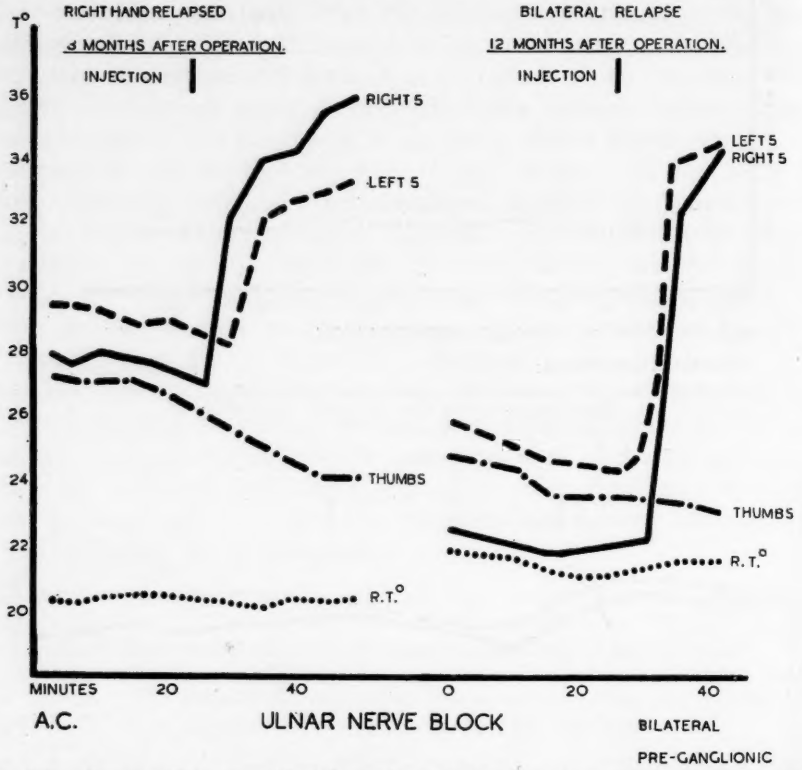

FIG. 172.—*Case* 8. Ulnar nerve-block 8 months after operation; vasodilatation is more evident in the right hand which has relapsed. At 12 months both hands have relapsed and vasodilatation is now identical.

of the right hand gradually deteriorated and her chilblains returned, so that the hand was as bad as ever, whereas the left hand was perfectly warm and satisfactory.

Anæsthetization of her ulnar nerves 8 months after operation revealed the presence of vasoconstrictor fibres in both nerves, but the vasodilatation obtained was more evident and gave a greater rise in skin temperature in the right hand, which had relapsed. Reflex sweating in this hand was easily elicited, whereas on the left hand only a little appeared between the fingers and on the webs. Water at 15° C. caused rapid cyanosis of the right hand, but the left hand preserved its normal good colour.

ON RE-ADMISSION.—She was re-admitted exactly a year after operation and stated that during the previous month the *left* hand had now begun to show attacks of cyanosis and had become cooler. On examination, both hands showed cyanosis, the right more than the left; both hands felt moist but the right hand was cooler than the left. Both hands for the first time had attacks of white spasm and showed the typical Raynaud phenomenon. Anæsthetization of the ulnar nerves showed a rapid and identical vasodilatation of the ulnar area of both hands, as shown in *Fig.* 172.

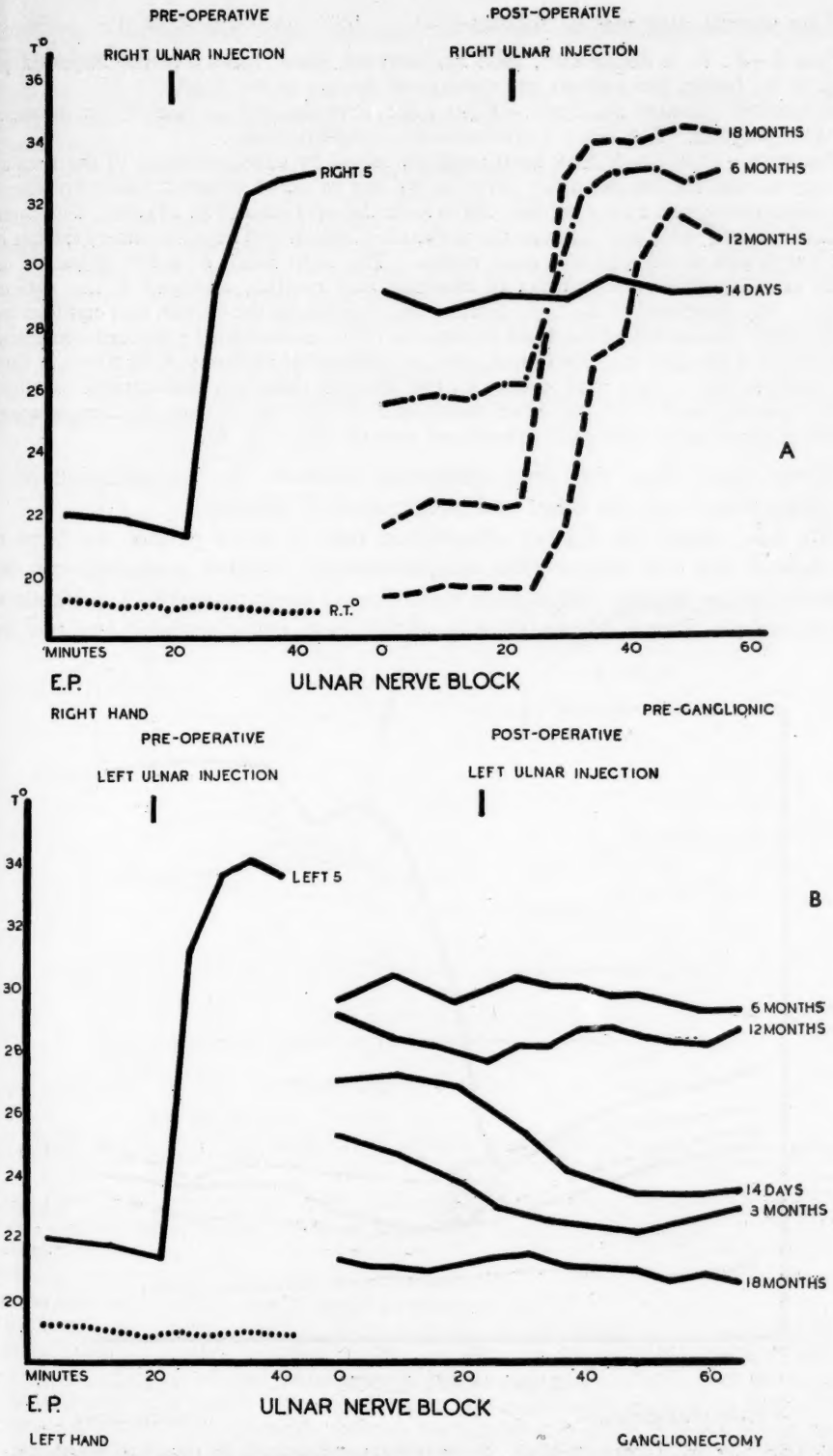

FIG. 173.—*Case* 9. A, Preganglionic section ulnar nerve-block. B, Ganglionectomy. The right hand showed clinical relapse 15 months after operation following the reappearance of vasoconstrictor fibres in the ulnar nerve. The left hand has not relapsed and vasoconstrictor fibres have not reappeared.

The second case was as follows :—

Case 9.—E. P., a dressmaker, aged 23, with ten years' history of the Raynaud phenomenon in the hands, but without any nutritional changes in the fingers.

OPERATION (January 19, 1937).—*Right side*: Preganglionic section of the thoracic cord below D.2 ganglion. *Left side*: Cervicothoracic ganglionectomy.

PROGRESS.—Both hands have been regularly tested by anæsthetization of the median and ulnar nerves, and the left hand has never shown any evidence of intact vasoconstrictor fibres in the ulnar nerve, nor in the median nerve since the operation (*Fig.* 173, B). This hand has remained perfectly well, and although the patient is a regular and keen swimmer, she has always found the fingers warm and of a good colour. The right hand, however, began to cool 15 months after operation and attacks of blueness and swelling appeared if the patient was worried. The condition of the hand deteriorated throughout the winter, and eighteen months after operation immersion of the hand in water at 15° C. immediately produced white and blue discoloration of the fingers. This hand gave no evidence of vasoconstrictor fibres in the ulnar nerve when tested 14 days after operation, but after six months a considerable vasodilatation followed anæsthetization of the ulnar nerve and seemed to increase in completeness and rapidity of appearance with each subsequent testing (*Fig.* 173, A).

These cases show the close correlation between the reappearance of vasoconstrictor fibres and the onset and progression of relapse.

We have made the further observation that in *every* patient we have tested who showed this late relapse after sympathectomy, whether postganglionic or preganglionic, a rise in skin temperature has followed ulnar nerve-block. Hands which have shown no clinical relapse after operation have never revealed any rise in skin

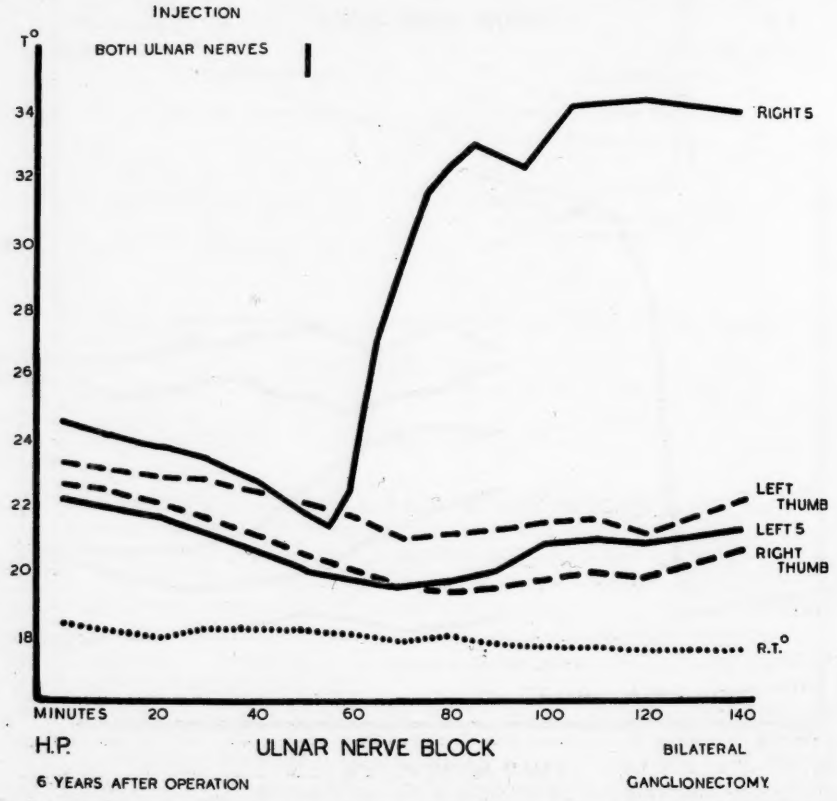

FIG. 174.—*Case* 10. Ulnar nerve-block. Six years after ganglionectomy the right hand has relapsed and shows the presence of vasoconstrictor nerve-fibres, which are absent on the left side which has not relapsed.

temperature, although the ulnar and median nerves were completely anæsthetized. The following cases illustrate this observation :—

Case 10.—H. P., aged 47, labourer, 2½ years' history of blueness in the hands when cold. No white spasm. Severe burning pain preventing work.

OPERATIONS.—

December 5, 1931.—Right cervicodorsal ganglionectomy.

October 29, 1932.—Left cervicodorsal ganglionectomy.

PROGRESS.—The man attended regularly for observation, and the hands remained well, keeping pink in cold water, until February, 1935, when he complained of unilateral sweating on the right side. Both hands were noted as being very well, but the right Horner was less.

In September, 1935, the right hand showed a little cyanosis.

In March, 1937, the right hand was cold and severely cyanosed, whereas the left hand was warm and of good colour.

On March 22, 1937, both his ulnar nerves were blocked with novocain and full vasodilatation was rapidly obtained in the ulnar area of the right hand, while no change was observed in the left hand, as shown in *Fig.* 174.

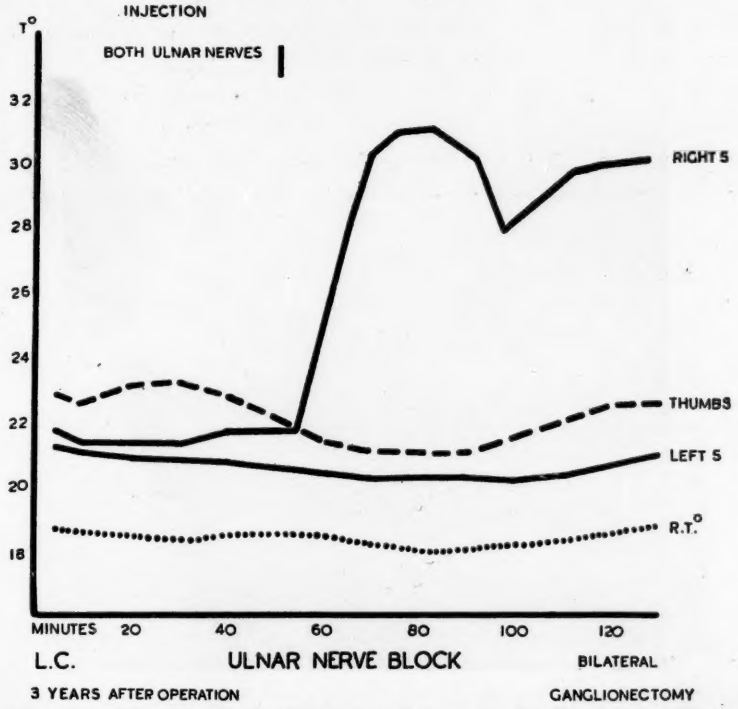

FIG. 175.—*Case* 11. Ulnar nerve-block. Three years after ganglionectomy the right hand has relapsed and vasoconstrictor nerve-fibres are present. None were detected on the left side which has not relapsed.

Case 11.—L. C., aged 30, coremaker, 12 months' history of typical Raynaud phenomenon in hands. Severe white spasm, but pain slight. No trophic lesions.

OPERATIONS.—

July 19, 1933.—Right cervicodorsal ganglionectomy.

January 20, 1934.—Left cervicodorsal ganglionectomy.

PROGRESS.—Both hands were extremely well after the operations, but 6 to 9 months later she noticed a gradual cooling and tendency to cyanosis on the right side. The hand was fairly satisfactory, but the next winter, January, 1935, she had white spasm of the tips of the fingers, lasting 20 minutes and more. The third winter the right hand was just as bad as before operation, and has continued so since, whereas the left hand is warm, of good colour, and has shown no sign of relapse.

Anæsthetization of her ulnar nerves gave a rapid and full vasodilatation of the right side and no effect upon the left side (*Fig.* 175).

These patients show on the left side a complete absence of relapse from 3 to 6 years after ganglionectomy, and the ulnar nerve-blocks reveal no evidence of vasoconstrictor fibres. On the right side, which relapsed gradually after an interval of 3 years in the first case and 6 to 9 months in the second, the ulnar nerve-blocks present clear evidence of the reappearance of vasoconstrictor nerves.

Regeneration will account for these findings, particularly in view of the remarkable power of regeneration of sympathetic nerves (Lee, 1930, Tower and Richter, 1931, 1932). On the other hand, it is not difficult to understand the

FIG. 176.—Radiograph showing the silver clips applied to the cut ends of the thoracic cord and the amount of separation obtained.

non-relapse of some cases because regeneration of nerves may not establish exact anatomical union, and still more often may show defects of physiological recovery—Ford and Woodhall (1938). Regeneration would also explain the several months of relief preceding relapse, and would account for the gradual progression of these symptoms when they appear. Furthermore, in the earlier preganglionic sections in which no definite attempt was made to prevent regeneration, signs of relapse appeared as early as three months after operation. This is much earlier than we have seen after ganglionectomy. The gap left by a preganglionic section, where no attempt has been made to separate the cut ends, is very small, and regeneration,

if it occurs, would be facilitated by the proximity of the intact postganglionic nerve-cells. For this reason Telford has stitched up the upper cut end of the sympathetic cord to the scalenus muscle in all recent operations, and silver clips have been applied to both ends of the cord. The clips have also enabled us to obtain a radiograph as a permanent record of the extent of the operation (*Figs.* 176, 177).

Theoretically it is more difficult to visualize regeneration after ganglionectomy. If all the postganglionic cell stations to the arm have been removed at operation

FIG. 177.—Radiograph showing silver clips applied to the cut ends of the lumbar cord and the amoun of cord removed and the levels of the section.

then either preganglionic fibres grow up and pass directly into the nerves of the brachial plexus, or, what appears to be more likely, postganglionic fibres, whose cell stations are situated *below* the level of excision, regenerate through the scar tissue to reach the nerves of the arm.

Although regeneration would seem therefore to be the deciding factor in the late recurrence of symptoms after operation, it does not exclude the possibility that the actual cause of the spasm is a local fault of the digital vessels which would persist despite operation (Lewis, 1938). The re-establishment of vasomotor tone by regeneration would precipitate spasm in such abnormal vessels, but not in cases where no local fault existed in the first place.

Furthermore, we have to consider the possibility of a progressive fault in the digital vessels which would overtake and nullify the vasodilatation produced by sympathectomy. We feel that this is more than a possibility, and that this does actually occur. In some of the late relapses the severity of the symptoms has appeared to be greater than we should have expected from the degree of vasodilatation obtained by the ulnar nerve-block. Since all our late relapses in the hands have shown the presence of vasoconstrictor fibres in the ulnar nerve, it has been impossible to differentiate the cases of relapse due to a progressive local fault in the vessels. In the following patient, however, relapse of the Raynaud phenomenon occurred in the feet, though we could detect no vasoconstrictor fibres in the posterior tibial nerve :—

Case 12.—M. H., aged 22, frame tenter. Two years' history of severe Raynaud phenomenon, both hands and feet, but the pain in the feet was severe and crippling.

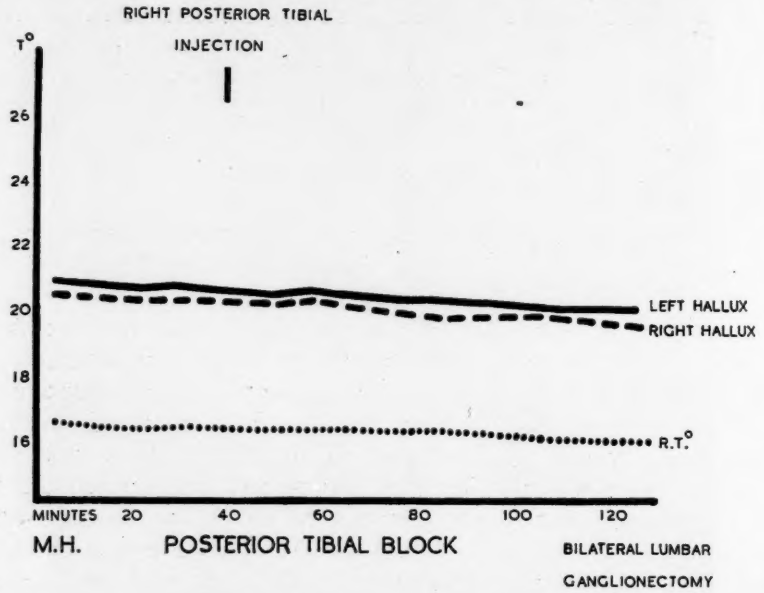

FIG. 178.—*Case* 12. Posterior tibial block showing the absence of vasoconstrictor fibres although clinical relapse has occurred.

OPERATION (April 14, 1934).—Bilateral lumbar ganglionectomy.

PROGRESS.—The next day the feet showed a rise of 10° C. in the ward over the pre-operative temperature. The feet continued in excellent condition until the winter of 1936, when they gradually became colder and showed transient attacks of white spasm and blue discoloration. When examined in February, 1937, both feet were cyanosed and felt extremely cold. She was admitted for investigation, and blocking of the right posterior tibial nerve with novocain produced no vasodilatation in the foot, the temperature remaining exactly similar to the left foot, which was used as a control. This result is shown in *Fig.* 178.

The absence of vasoconstrictor fibres in this case which has shown progressive relapse, commencing eighteen months after operation, suggests the presence of a progressive local fault in the blood-vessels which has overtaken and nullified the dilatation produced by the presumably complete sympathectomy. This is an isolated case and we feel that the most important factor in the causation of late relapse after sympathectomy is the regeneration of vasoconstrictor nerve-fibres.

The following tables present a complete analysis of the 38 ganglionectomies and 29 preganglionic sections which have been investigated in this inquiry:—

GANGLIONECTOMIES

Disease	Incomplete Operation	Early Relapse	Late Relapse	No Relapse	Unknown	Totals
Acrocyanosis	1	—	4	2	—	7
Raynaud	2	1	10	2	1	16
Raynaud with sclerosis	1	4	5	—	—	10
Scleroderma	—	4	1	—	—	5
Totals	4	9	20	4	1	38

PREGANGLIONIC SECTIONS

Disease	Incomplete Operation	Early Relapse	Late Relapse	No Relapse	Unknown	Totals
Acrocyanosis	1	—	4	—	—	5
Raynaud	—	1	8	7	—	16
Raynaud with sclerosis	—	3	5	—	—	8
Scleroderma	—	—	—	—	—	—
Totals	1	4	17	7	—	29

The Raynaud with sclerosis group of cases is composed of those cases of the Raynaud phenomenon which showed evidence of trophic and nutritional changes in the fingers, whereas the Raynaud group is limited to uncomplicated cases of that condition. The five cases of scleroderma all had the Raynaud phenomenon at some time in the history of their disease, but in all of them the sclerosis was the main condition, and it was not limited to the fingers, but affected the face, ears, upper part of the chest, and even the forearm and arms in the most severe cases. The tables show a high incidence of early relapse in scleroderma and in Raynaud cases complicated by sclerosis. Out of the total of 13 cases of early relapse treated by either operation, no less than 11 had sclerosis and nutritional changes in the fingers, and the 2 remaining cases had had the Raynaud phenomenon for many years. All the cases in the sclerosis and scleroderma groups eventually relapsed and this would suggest that sympathectomy is not worth doing for these conditions. The operation certainly has no beneficial effect when the disease is advanced, but the less severe cases all insist that the operation has made them much more comfortable and has been well worth while, although, objectively, there is not much improvement in the condition. Late relapse, which we suggest is due to regeneration, also has a high incidence, appearing in over 50 per cent of cases after either operation, and particularly interesting is the frequency of its occurrence in the acrocyanosis and uncomplicated Raynaud cases.

Lewis (1938) stated that the preganglionic operation had not solved the problem of the recurrence of symptoms after operation, and we have found that early and late relapse do occur after both operations, but, nevertheless, the preganglionic sections show better results than the ganglionectomies. They have been

performed more recently, but clinically they are undoubtedly better, the hands never relapsing to the severe degree which we have seen occur in some of the ganglionectomies. The absence of the Horner syndrome is also a distinct advantage, though many of the ganglionectomies have lost this syndrome after a few years, again suggesting regeneration of sympathetic nerve-fibres.

We have taken the slightest attack of cyanosis to mean relapse, although the patient may not have attached any importance to it, so that our figures do not in any way reflect the patient's evaluation of the operations. The majority of patients who have had the preganglionic section and many of those who have had ganglionectomy are completely satisfied with the result and grateful for the performance of the operation.

CONCLUSIONS

In reviewing 38 ganglionectomies and 29 preganglionic sections of the thoracic cord performed in Professor Telford's clinic since 1931, we have established the following points :—

1. Both types of operation are liable to be followed by relapse, and when it occurs it appears at an earlier date after preganglionic section than after ganglionectomy.

2. Excluding cases of incomplete denervation, the relapses fall naturally into two groups :

a. Those in which symptoms recur within a few days of operation—or would be manifest at this time if tested objectively by immersion in water at 15° to 18° C.

b. Those in which relapse does not appear for several months and which we have designated ' late relapse '.

3. The first group of early relapses are due to a local fault in the digital vessels which is sufficiently severe to nullify the effectiveness of the vasodilatation obtained by the sympathetic denervation.

4. The second group of late relapses cannot be accounted for by the hypersensitivity of the denervated blood-vessels to circulating adrenaline. This hypersensitivity diminishes with time and is less evident, or may be completely absent, when clinical relapse becomes apparent.

5. In all our arm cases relapse has been accompanied by a regeneration of vasoconstrictor fibres. The reappearance of these nerves has been first observed when, or shortly before, clinical relapse has become apparent. In certain patients it has been possible to predict with success a clinical relapse by the discovery of regenerating vasoconstrictor fibres in the ulnar nerve. The symptoms of relapse when manifest become steadily worse and at the same time there is a gradual increase in the degree of vasodilatation obtained by anæsthetization of the ulnar nerve.

It seems highly probable, therefore, that regeneration of vasoconstrictor nerve-fibres is the cause of late relapse after sympathectomy.

6. A progressive local fault in the digital vessel may produce a late type of relapse.

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ACTINOMYCOTIC AND MYCOTIC LESIONS, WITH SPECIAL REFERENCE TO 'MADURA FOOT'

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ACTINOMYCOSIS is not a rare disease, and since the days of Bollinger and Harz in 1877 the subject has attracted the attention of many workers, and a large number of facts has been accumulated. More recently the work of Naeslund (1931) has added considerably to our knowledge of actinomycosis, and Zachary Cope (1938) has given an excellent all-round review of the subject.

The aerobic type of this group of organisms is mainly distributed in the soil, and since India is largely an agricultural country where the people are in close contact with the soil, any information about this disease in India is worth considering. We record the facts which we have gathered from the study of material from the surgical section of the Department of Pathology and Bacteriology of the Calcutta Medical College collected over a number of years. In addition we describe in detail three recent cases of Madura foot.

Unfortunately the old records are incomplete, but we have been able to collect 32 cases, including the 3 cases described below, and in most of these the diagnosis has been confirmed histologically. The findings are summarized in *Tables I–V*.

When considering the tables the following points should be borne in mind:—

1. The sex incidence shows 16 males in 22 cases, but this figure may be misleading, since males form the bulk of patients seeking hospital aid.

2. Similarly as regards religion, since Hindus greatly outnumber Mohammedans and patients of other religions.

3. Unfortunately the old records do not mention the patients' occupations, but from a study of the history sheets and from our personal experience of the majority of our hospital patients, we feel certain that the cases mostly belong to the working class.

4. As regards distribution, the foot is the most commonly affected site, comprising 23 out of a total of 32 cases. Two cases of primary actinomycosis of the breast are included in the series. These have already been recorded—De and Chatterjee (1934) and Roy and Tribedi (1938), the latter being the tenth case on record of this very rare type. Another uncommon case, one of primary actinomycosis of the sigmoid colon, is also included.

5. Unfortunately the old records make no reference to the exact type of the organism. The cases are recorded as black or red according to the colour of the granules, and this has been shown by Boyd and Crutchfield (1921) to be insufficient for classification.

Table I.—Summary of 32 Cases at the Medical College, Calcutta

Serial No.	Age	Sex	Religion	Site of Lesion	Duration of Illness
1	21	F.	—	Jaw	3 years
2	—	—	—	Lower jaw	—
3	35	F.	H.	Right breast	8 years
4	30	M.	H.	Back, skin	—
5	15	F.	H.	Left iliac fossa	—
6	—	—	—	Right hand	—
7	—	—	—	Right hand	—
8	35	M.	M.	Left arm	—
9	40	M.	H.	Right foot	11 years
10	35	M.	H.	Right foot	—
11	25	M.	M.	Right foot	2 years
12	—	—	—	Right foot	—
13	50	M.	—	Right foot	5 years
14	—	M.	H.	Right foot	2 years
15 (*Case* 3)	40	M.	H.	Right foot	12 years
16 (*Case* 1)	35	M.	M.	Right foot	9 years
17	—	F.	H.	Left foot	10 years
18	Adult	M.	M.	Left foot	—
19	—	—	—	Left foot	—
20	—	—	—	Left foot	—
21 (*Case* 2)	55	M.	M.	Left foot	4 years
22	50	F.	H.	Left foot	1 year
23	—	M.	—	Foot	3 years
24	—	—	—	Foot	—
25	—	—	—	Foot	—
26	—	—	—	Foot	—
27	—	—	—	Foot	—
28	45	M.	H.	Foot	—
29	37	M.	H.	Foot	3 years
30	28	M.	H.	Right foot	3 years
31	35	F.	H.	Right breast	1 year
32	50	M.	H.	Left foot	8 months

Table II.—Distribution of Lesions

Jaw	2
Right breast	2
Back, skin	1
Left iliac fossa	1
Arm	3
Foot	23

Table III.—Age Incidence

10 years and under	0	
Between 11 and 20 years	1	
Between 21 and 30 years	4	18
Between 31 and 40 years	8	
Between 41 and 50 years	4	
Between 51 and 60 years	1	
Not recorded		14

Table IV.—Sex Incidence

Male (M.)	16	22
Female (F.)	6	
Not recorded		10

Table V.—Incidence regarding Religion

Hindu (H.)	14	19
Mohammedan (M.)	5	
Other religions		0
Not recorded		13

The 3 cases we have recently had an opportunity of completely investigating are described in detail below.

CASE REPORTS

Case 1.—J. K., aged 35 years, Mohammedan male, inhabitant of Kabul, came to the hospital for inability to use the right foot owing to a large irregular swelling occupying the posterior part of the sole and lateral part of the right foot.

HISTORY.—The patient first noticed a painful pea-like body on the posterior part of the sole of the right foot nine years ago. The swelling went on increasing, and a number of similar pea-like bodies appeared near the original one. Thus the whole of the leg became swollen. Later, a sinus appeared in one of the pea-like bodies, from which sanguineous discharge issued.

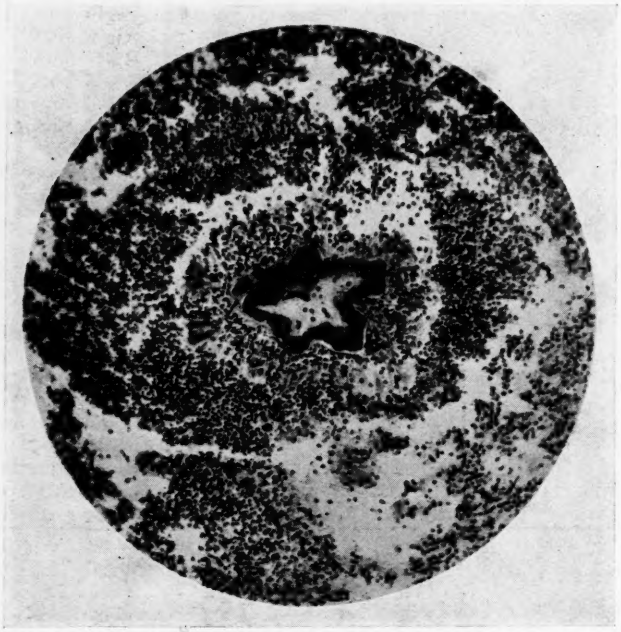

FIG. 179.—Photomicrograph (low magnification) of a section from *Case* 1 (ochroid type), showing the actinomycotic 'druse' with characteristic club formation.

Following an operation for varicose veins two years ago his condition improved, but the foot gradually became worse and ultimately useless.

ON EXAMINATION.—The swelling was found to be studded with pea-like nodules, some of which were ulcerated and exuded blood, pus, and granular bodies on squeezing.

On cultural examination of the granules, an actinomyces was obtained which conformed to the variety of *Actinomyces maduræ*. The material from biopsy revealed the typical appearance of an actinomycotic 'druse' (*Fig.* 179).

TREATMENT.—The patient was treated with six exposures of deep X-ray therapy, which somewhat improved the condition of the wound but increased bleeding was noticed.

Case 2.—Mohammedan male, aged 55 years, a cultivator by occupation, noticed a gradually increasing swelling of the ankle-joint of the left foot for the last four years. On examination, the whole foot was found to be swollen and with a number of ulcerated discharging areas. The leg was amputated. Cultures from different portions of the sagittal section of the foot grew *Actinomyces maduræ* and *Staphylococcus aureus*.

This is the so-called ochroid or pale variety of mycetoma due to infection with *Actinomyces maduræ*, complicated with a secondary staphylococcal infection. A sagittal section through

the foot shows that all the tissues—subcutaneous, muscular, and osseous—were extensively involved (*Fig.* 180), the process of destruction was more marked, and multiple pits of various sizes could be seen, some of them containing cheesy material which on examination was found to be staphylococcal pus. The numerous foci of infection presented areas of different colours —grey, yellow, brown; in some of the areas white and brown pigments could be seen at the same time. The degree of pigmentation evidently indicated the age of the colonies, the earlier being grey and the older ones producing brownish pigments.

Histological examination revealed the typical picture of actinomycotic 'drusen'. There is a central necrotic area surrounded by a zone of bacteria enclosed in the characteristic clubs. This again is surrounded by a mass of inflammatory cells bounded by a zone of fibrous tissue.

FIG. 180.—*Case* 2. Sagittal section of the foot, showing the ochroid variety of mycetoma.

Case 3.—A. K., aged 40, Hindu male, unemployed, came to the hospital for the relief of a gradually increasing swelling of the right ankle and foot, which was tender and painful.

HISTORY.—He first noticed the condition twelve years ago, with occasional pain in the right foot accompanied by fever. The swelling appeared a few months later. This acute stage was followed by a more or less quiescent period, followed again by another febrile and painful attack. The swelling gradually increased, and three years ago a sinus appeared from which an intermittent discharge was noticed.

ON EXAMINATION.—There was a swelling around the right ankle-joint involving the posterior part of the dorsum of the right foot. The skin was black and tense and there were four healed ulcers on the medial aspect of the swelling.

X-ray examination showed fairly extensive patchy absorption of the tarsal bones; there was a good deal of periosteal reaction.

The amputated foot was sectioned sagittally and presented an interesting picture (*Fig.* 181). To the casual observer it presents an appearance of charcoal being scattered over the cut surface of the foot. The involvement of the tissues is extensive, attacking all the elements, but no black patches are seen in the subcutaneous tissues. In this case the destructive changes are less than in *Case* 2, and actual cavity formation is surprisingly absent even after a history of twelve years. Each area is composed of an intense black irregular central zone, surrounded by a pale whitish ground-glass-like area. On squeezing, hard, brittle, black granules resembling charcoal came out.

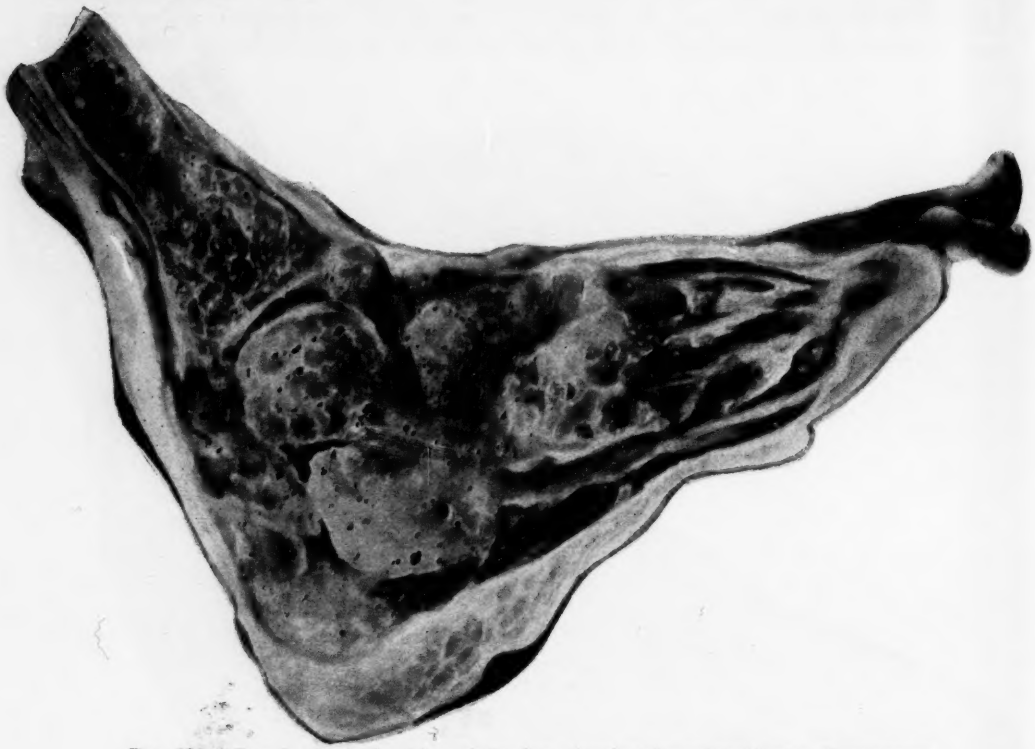

FIG. 181.—*Case* 3. Sagittal section of the foot, showing the melanoid type of mycetoma.

Bacteriological examination of the material collected from the amputated foot yielded a filamentous growth, with production of hyphæ having the characters of a hyphomycete; lateral and terminal buddings were noticed, but there was no true branching. Cultural characteristics were as follows: a luxuriant growth in nutrient agar and in enriched media; the earlier growths on solid media appeared as white star-shaped woolly colonies with a central black area; black pigmented growth appeared in older cultures, and in eight weeks a thick velvety pigmented growth was obtained (*Figs.* 182–184). Ordinary laboratory carbohydrates and alcohols were fermented without the production of gas. In liquid media a puff-ball-like growth appeared in earlier cultures which became pigmented later (*Fig.* 185). Intraperitoneal, intramuscular, and subcutaneous inoculation into rabbits and guinea-pigs were without any results.

Histological examination showed that the central part of the nodule is composed of mycelia, but there is no pigmentation. The peripheral part of the colony is composed of hyphæ of different size and of a black pigment (*Figs.* 186–188). Stained with hæmatoxylin and eosin, the pigments appear deep brown and with Gram-Weigert's stain they appear black. Surrounding this pigmented fungal layer there are leucocytes, mainly polymorphs, but no clubs (*Figs.* 187, 188). The ground-glass-like area as described before was composed of this cellular layer, as seen in *Fig.* 187.

FIG. 185.—Material from the same case in serum broth (1 week old).

FIG. 184.—The same growth (8 weeks old).

FIG. 183.—The same growth (3 weeks old).

FIG. 182.—Culture in serum-agar media (1 week old).

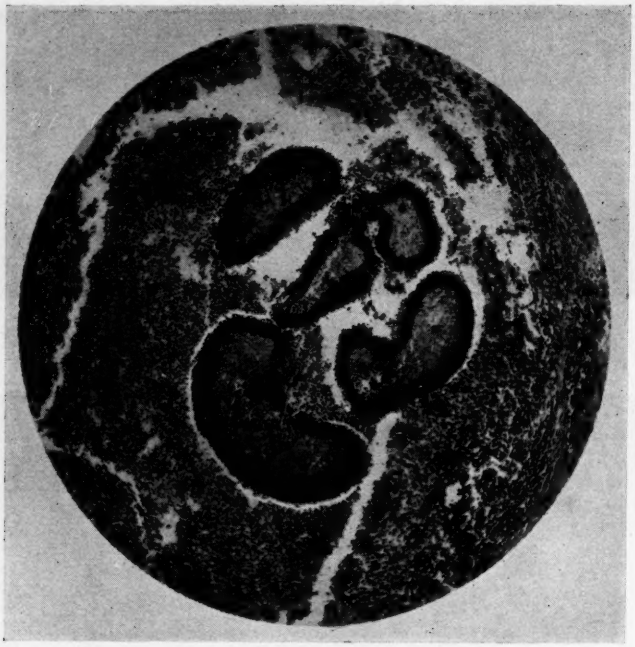

FIG. 186.—Photomicrograph (low magnification) of a section from the melanoid type of mycetoma, showing four fungal colonies.

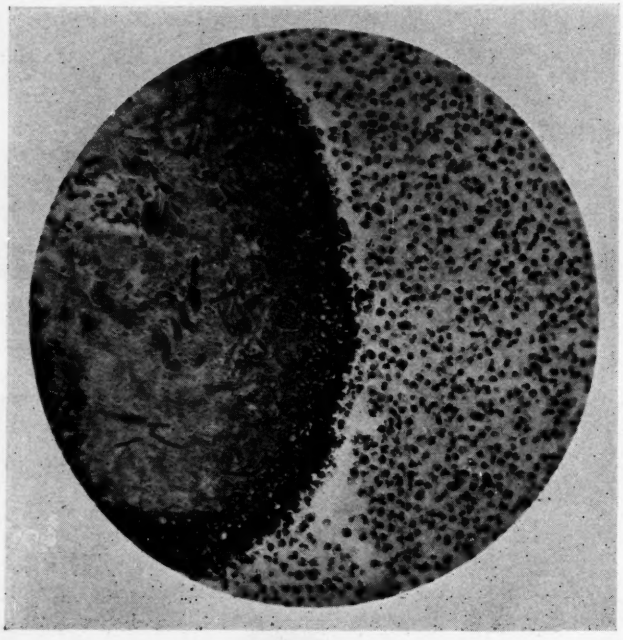

FIG. 187.—Photomicrograph (high magnification) of a portion of *Fig.* 183. Note the typical fungal mycelia with the peripheral pigmented layer, the absence of actinomycotic clubs, and the absence of round cells and plasma cells; but the polymorphonuclear reaction is marked around the fungal colony.

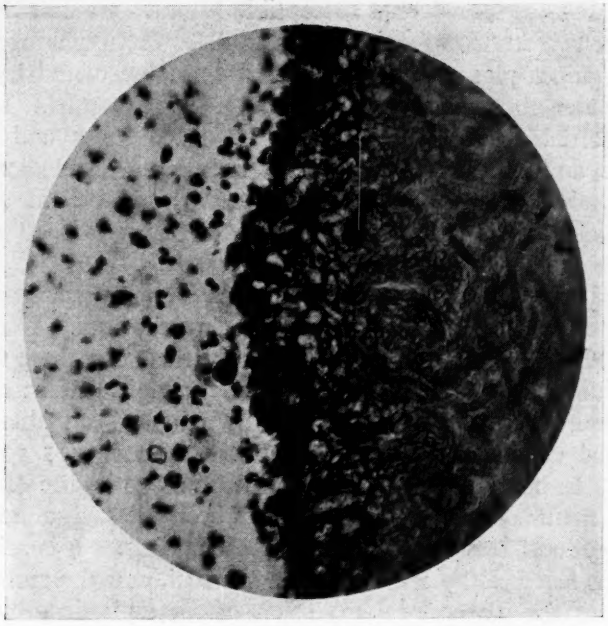

FIG. 188.—Photomicrograph (higher magnification) showing a portion of *Fig.* 184 in more detail.

DISCUSSION

'Mycetoma', 'Madura foot', 'Maduramycosis', and 'Madurosis' are the usual names that are given to this type of affection of the foot. The condition is almost confined to tropical countries and is mainly found in the working-class population who do not have the protection afforded by shoes.

The association of injuries, noticed or unnoticed, of the bare feet with the distribution in the soil of the causative organism accounts for the frequency of the foot infection. Since other parts of the body may be primarily involved there seems little justification for retaining the name Madura foot as a separate clinical entity, although it has the sanctity of history (Colebrook, 1846, and Vandyke Carter, 1860).

In *Cases* 1 and 2 the organisms isolated belonged to the aerobic group of actinomyces and conformed to the type of *Actinomyces maduræ* described by Topley and Wilson (1936). The organism of the third case was a hyphomycete, giving rise to the so-called melanoid type of mycetoma which we have described in detail because of its rarity. Wright (1898) described a case in an Italian woman which was reviewed by Boyd and Crutchfield (1921). Gammel, Misdjian, and Thatcher (1926) described only 1 case of this type, in a Mexican, out of 20 cases they studied, but their case did not show the same involvement of bone and muscle. Our two actinomycotic cases yielded organisms which grew aerobically. Zachary Cope (1937) is sceptical about the pathogenic role of the aerobic group of actinomyces, and lays down the criterion of pathogenicity in experimental animals as the proof of infection. We, however, hold that mere failure of this test cannot be taken as a proof that the organism is not the causative factor. Such is the case in leprosy

and many virus diseases for which a susceptible laboratory animal has not yet been discovered. Our two strains of actinomyces and also the hyphomycete from *Case* 3 failed to infect guinea-pigs and rabbits which were inoculated by various routes and were kept under observation for from four to eight months. In all three cases we collected material from more than half a dozen areas and subjected them to both aerobic and anaerobic cultural methods and histological examinations, with uniform results. It therefore appears quite justifiable to state that these organisms were responsible for the condition, though they failed to infect laboratory animals.

The external appearances of the three cases were typical of mycetoma, viz., general swelling of the foot with sinuses, excluding the toes. With regard to the internal changes, Boyd and Crutchfield (1921) remarked that there were disappointingly few descriptions of the internal gross or microscopical tissue changes, scarcely half a dozen observations being on record. We have been able to describe in detail the internal changes in the last two cases. In *Case* 1 we only obtained biopsy material. In both types (actinomycotic and mycotic) the distribution of the foci is patchy in nature. From a close study of both the sagittal and cross-sections of the feet, it is found that the process of invasion is not a continuous one, but there are more or less healthy areas between the foci, and the spread of the lesion is not like that of the direct local extension of a neoplastic growth. It is now accepted that club formation is definitely a cellular reaction of the tissues of the host and is not a part of the organism (Topley and Wilson, 1936); hence it appears that the tissue reactions are different in actinomycotic and mycotic infections of the foot—in the former club formation is quite marked, whereas in the latter it is entirely absent. Moreover, the accumulation of round cells, fibroblasts, and plasma cells was greater in the bacterial than in the mycotic mycetoma. The polymorphonuclear leucocytic reaction was, however, more marked in the mycotic infection.

SUMMARY AND CONCLUSIONS

1. Thirty-two cases of actinomycosis collected from the records of the Calcutta Medical College are classified.

2. Three recent cases of affection of the foot, two actinomycotic and one mycotic, are described in detail.

3. The mode of infection, bacteriology, morbid anatomy, and histology of the above cases are discussed.

4. The difference in tissue reactions between the bacterial and fungal types of mycetoma are noted.

Our thanks are due to Dr. M. N. De, Professor of Medicine and late Professor of Pathology, Medical College, Calcutta, for his critical suggestions; to Dr. G. Galstaun, Professor of Radiology, for radiographing the foot; and lastly to the Staff of this Department for the ungrudging help rendered.

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SILENT HYPERNEPHROMATA

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It is a well-recognized fact that the first warning of malignant disease in the body may come from a metastasis or secondary deposit, and not from the primary growth itself. In cases where this condition arises we may take it that the symptoms of the primary disease have been in abeyance, or else have been so slight as to have escaped the notice of the patient. If a portion of the metastasis can be obtained for microscopical examination the way of diagnosis is made easy, but if the metastasis occurs in a deep-seated position, or is so inaccessible that a biopsy cannot be done, diagnosis may prove difficult and the real nature of the case be overlooked. In fact it is not unknown for a metastasis to have caused death before the primary neoplasm was discovered or even suspected.

Metastases which declare themselves while the parent tumour sleeps, as it were, are most frequently associated with neoplasms of such organs as the thyroid, adrenal, and kidney. In these the vascular supply is particularly favourable for the dissemination of new growths, and cell emboli are transported in the blood-stream to distant parts to originate secondary tumours. It is not surprising, then, to find metastases a common complication of that commonest of all kidney tumours—the hypernephroma. What is not perhaps so generally realized is that in cases of hypernephromata it is by no means rare for a metastasis to appear as the first evidence of the disease. Below are recorded two cases which exemplify this. There was no history of renal or urinary symptoms in either case. In the first case the metastasis showed itself as a fungating tumour of the scalp, and on microscopic examination the tissue was found to be typical of hypernephroma. This patient went downhill rapidly, though at the time a tumour was not palpable in either kidney. In the second case the metastasis occurred in the cerebellum, but the patient had in addition a large tumour of the right kidney of which he was unaware. Both tumours in this case were removed, and now six years afterwards the patient is alive and well. Full details are given on pp. 269–272.

CLINICAL FEATURES

Hypernephroma, sometimes called Grawitz tumour and in more recent times carcinoma of the renal cortex, is, as already mentioned, the commonest neoplasm of the kidney, for it is estimated that 80 per cent of all tumours of the kidney are hypernephromata. The classical symptoms of the condition are pain, tumour, and hæmaturia. Exception is taken by some authorities to the term ‘classical’, on the grounds that it is misleading for the student. No doubt the latter is so burdened with the detail required for examinations, that any symptoms so outstanding as to be called ‘classical’ make a distinct appeal. The danger is that he may be too trusting, and expect to find the main features in every case. Nowadays, however,

urologists teach us that all three symptoms are present together only late in the course of the disease, long after the diagnosis should have been made. In fact in their opinion this triad of symptoms is classical to the extent of being obsolete. They insist that pain or hæmaturia should not wait on tumour formation, and that either of these symptoms, no matter how slight, should start a series of investigations that ends only with the discovery or elimination of the disease.

An interesting study of the chief symptoms and the frequency of their occurrence in hypernephroma has been made by Judd and Hand. They reviewed in all 367 cases at the Mayo Clinic, and their conclusions were briefly as follows: *Pain* was the initial symptom in 37·32 per cent of cases, but was eventually complained of in more than 80 per cent. *Tumour* was the first symptom in 13·62 per cent only of cases, although about four-fifths, or 80 per cent, of the patients had palpable tumours at the time of examination. *Hæmaturia* was the first symptom in 43·86 per cent. It was present in 69 per cent of cases at some time in the course of the disease, which means that altogether it failed to make its appearance in 31 per cent. *Weakness* was recorded as the first symptom in 3·26 per cent. *Fevers* and *anæmia* are also mentioned, but the percentage of cases in which these were the first symptom is not given.

Pain, aching in character, is mostly localized to the renal area, and in many cases is due to mechanical interference with drainage of the kidney. Acute attacks of pain in the renal area are most probably due to hæmorrhage into the tumour itself, but if severe pain is referred down the ureter to the bladder and genitalia it is probably due to the passage of clots, though the colic in these cases is held to be less than that due to stone. It has been said that growths of the upper pole of the kidney give rise to pain as an early symptom owing to interference with the diaphragm, but Wright, who made a most careful study of cases at the Royal Cancer Hospital, could not find evidence to substantiate this opinion.

It is a noteworthy fact that a patient may harbour a large and easily palpable *tumour* and be unaware of its presence. According to Ljunggren a tumour of the kidney to be palpable must be as large as a man's fist unless it is situated on the anterior surface of the lower pole, or the patient is emaciated. Some hold that hypernephromata occur more frequently in the upper pole of the kidney, but in the Mayo Clinic series the tumour was found much more commonly in the lower pole and midrenal region. One would expect tumours of the lower pole to come to light earlier than those of the upper, inasmuch as they are more accessible to palpation and are more likely to interfere with drainage of the renal pelvis. Judd and Hand say the larger the tumour the shorter the post-operative life. In their series immediate risk of operation proved greater if the tumour was large, and patients in whom the tumour was small lived considerably longer than those in whom the tumours were of moderate or large size.

Hæmaturia may be gross or it may be so negligible as to escape notice. Wright states that the milder degrees of hæmaturia are due to venous congestion, pressure of the advancing growth blocking the smaller veins while the lumen of the arteries remain intact. Small hæmorrhages then take place into the neighbouring tubules and the blood is intimately mixed with the urine. Smoky urine may or may not be observed by the patient, but routine examination of the urine would no doubt disclose blood in many cases where the patient failed to notice any change. Profuse hæmaturia is due to involvement of the renal pelvis by the tumour and is followed

by renal colic due to the passage of clots. Jocelyn Swan draws attention to the influence which the site of the tumour may have on the incidence of hæmaturia. A tumour whose origin is close to the renal pelvis may early on involve a calix and give rise to hæmaturia, whereas a tumour at the periphery of the cortex may grow to a large size without causing this symptom.

Repeated hæmorrhages will no doubt give rise to anæmia, but anæmia may be due in a measure to the malignant disease itself. A marked degree of anæmia will militate against the success of operative measures unless it be corrected by treatment, which will include blood transfusions.

Fevers, chills, and night sweats were present in 10 per cent of the Mayo Clinic series, and it was assumed that these were due to pyelonephritis. Israel found fever to be a characteristic in more than half his cases. He observed fever curves, remittent and intermittent, and believed that temperature in a great many cases occurred apart altogether from infection. This may be due as Wright suggests to the entrance into the blood-stream of small amounts of foreign protein detached from the growth, and is anaphylactic in nature.

METASTASES

There still remain those cases in which the tumour progresses silently without giving rise to symptoms and the first thing to call attention to the disease is a metastasis. The primary tumours in such cases might, for want of a better term, be called ' silent hypernephromata '. Opinions differ as to the percentage of cases in which a metastasis is the first sign. Deuticke found it to be 9 per cent, and Israel as high as 50 per cent. Creevy, aware of the findings of both those authorities, made a special study of 92 cases of metastases—clinically and post mortem—and found the percentage to be 41 per cent of the whole group—a remarkably high figure.

From published reports it would appear that the metastases of hypernephromata have been found in almost every part of the body, sometimes in the most unexpected places. According to Judd and Hand the commonest sites in order are the lungs, liver, bones, and central nervous system. In Creevy's series the bones were most frequently involved. Lehmann, who studied a series of 50 cases of bony metastases, found that the flat and long bones were more or less equally affected; they occurred in the sternum, clavicle, vertebræ, scapula, humerus, ulna, femur, tibia, and tarsus. In the majority of cases invasion is through the blood-stream, but in some it would appear to travel by way of the lymphatics. In Gordon Simpson's series—admittedly small—the vertebræ were affected in every case, but it was significant that invasion was confined to the 1st, 2nd, and 3rd lumbar vertebræ, suggesting local spread from lymphatics. In support of this view he quoted in addition one of Sir John Fraser's cases, in which one-half of the first lumbar vertebra was involved—that half on the side of the affected kidney.

In the bones the first sign of a metastasis may be swelling, or in the case of the long bones a pathological fracture. Pain attributed to rheumatism is frequently complained of, but the pain of vertebral involvement may be very severe, as Simpson found in his cases, though in all of these it must be added there was collapse of one or more vertebræ. In the lungs shortness of breath and cough are significant. There is a danger, of course, that in spite of careful examination and X-ray investigation such cases, in the absence of a biopsy, may be mistaken for primary growths

of the lungs or bones, for tuberculosis, for gummata, and so on. Creevy states that when a lesion in the lung becomes evident the primary tumour has usually attracted attention, but cases are on record where patients were under treatment for long periods for pulmonary disease, and the correct diagnosis was only eventually reached when sections were made from portions of tumour coughed up or obtained by bronchoscopy. It is to be noted that in Lehmann's series, the number of cases in which a solitary metastasis was mistaken for the primary lesion of bone, before biopsy, is remarkably high. It sometimes happens, however, that a metastasis or secondary tumour has been suspected or correctly diagnosed as such while the primary focus has remained undetermined. An example is one of Shinz's cases, in which a secondary deposit in bone was thought to be a metastatic seminoma, but when it failed to respond to radiation therapy a tentative diagnosis of hypernephroma was made. This was later verified at autopsy. In Shinz's other cases—9 in number—3 were correctly diagnosed because of previous nephrectomy for hypernephroma, 3 after biopsy, and 3 at autopsy.

The figures given by Creevy and Israel serve to emphasize the supreme importance of an early diagnosis if the disease is to be forestalled, and they serve as a warning that in this disease there is no symptom so trivial that it can be neglected. There is much to be said for the American system which encourages patients to report periodically for examination and X-ray overhaul. The introduction of solutions such as uroselectan and diotrast in X-ray of the urinary tract has helped enormously; excretion of the dye is a measure of the function of the kidney, and its outlining of the pelvis and calices draws attention to any filling defect or distortion. The investigation causes the patient little inconvenience and only in case of doubt is it necessary to supplement the examination with a retrograde pyelogram. Furthermore, as metastases are a common complication of this disease, it would appear that in the case of the discovery of a renal neoplasm, no investigation can be considered complete which does not include radiographs of the lungs and the commoner bony sites for metastases.

CASE REPORTS

The following are the records of the two cases already referred to. (The specimens of *Case No.* 2 are in the Museum of the Royal College of Surgeons.)

Case No. 1.—A female patient, aged 50, was admitted to the North Middlesex Hospital, on Oct. 24, 1923, bleeding from a fungating tumour of the scalp. The hæmorrhage was a steady ooze and had been in progress for about four hours. The tumour was roughly 2–3 in. square, and was situated in the right frontal-parietal region. Forceps would not hold in the friable tissue, and the hæmorrhage was arrested by tying a rubber catheter around the scalp, above the orbits, ears, and occiput, and fixing it in position with sutures. The main vessels supplying the tumour were exposed and ligatured, and the tumour was removed. The tumour involved almost an equal area of the bone beneath, but did not penetrate the dura. The section was sent to Dr. W. W. Woods, of the London Hospital, who reported that the tissue was typical of Grawitz tumour or hypernephroma, and was no doubt a metastasis. There was no history of renal or urinary symptoms, and no tumour of the kidney could be felt. The lower pole of the right kidney was palpable, but this was not remarkable as she was a spare women, above medium height. She refused, however, to have any further investigations or operation done, and left hospital before her wound had healed. She returned six months later in a moribund condition. Permission was given for a limited post-mortem examination which showed the right kidney almost completely replaced

by growth, with extensive secondaries in lungs and pleuræ. There was no recurrence at the site of the original metastasis.

Case No. 2.—A male patient, aged 60, was admitted to the Hospital of St. John and St. Elizabeth, on July 10, 1933. For four weeks he had suffered with intermittent headache, which was always worse at night and in the early morning. He occasionally felt sick, but had vomited only once. For six weeks he had some difficulty in walking, especially in maintaining his balance when erect. This disability led to a fall in which he sustained a head injury. The history of his injury was at first misleading and for a time was wrongly held to be responsible for his symptoms. The patient, who was a strict teetotaller living in a country district, was conscious that gossip credited his unsteadiness of gait to the use of alcohol.

FIG. 189.—*Case* 2. A, Renal tumour. B, Cerebellar metastasis.

ON EXAMINATION.—A large swelling was discovered in the right loin. It was painless and solid. Intravenous uroselectan showed that while the left kidney was functioning normally, and there was no enlargement of the calices or pelvis, no dye at all was seen in the right kidney. There were no urinary symptoms, nor could the patient remember having suffered from urinary trouble. In view of the finding of this tumour and my experience with the previous case, I began to have doubts as to the nature of the head injury already mentioned, and to suspect that the patient's symptoms might be due to a secondary deposit in the cerebellum. Radiography of the skeletal system for metastases was negative.

Nervous System.—Dr. Gordon Holmes reported as follows: "Visual acuity and the visual fields were normal, but there was early papillœdema in both eyes. The ocular movement, slow on deviation to the right, more rapid to the left. His pupils reacted to light and on convergence. There was a slight degree of loss of sensation on the left trigeminal area, and the left side of the face moved a little less than the right, but this may not have been pathological. There was some deafness in the left ear. There was a considerable amount

of cerebellar dysarthria. There was no loss of power in any of the limbs, but tone was reduced in the right arm and leg, and there was considerable inco-ordination in movement in these limbs. He was unable to perform alternate movements rapidly with either arm, but succeeded in this test better on the right than on the left. All his reflexes were brisk but the plantar responses were flexor." In Dr. Gordon Holmes's opinion, the symptoms were due to a tumour of the cerebellum near the middle line, probably projecting more to the right than to the left side.

FIRST OPERATION (July 24, 1933).—Right paramedian incision supplemented by a transverse incision of the rectus muscle through a linea transversa. The large intestine was

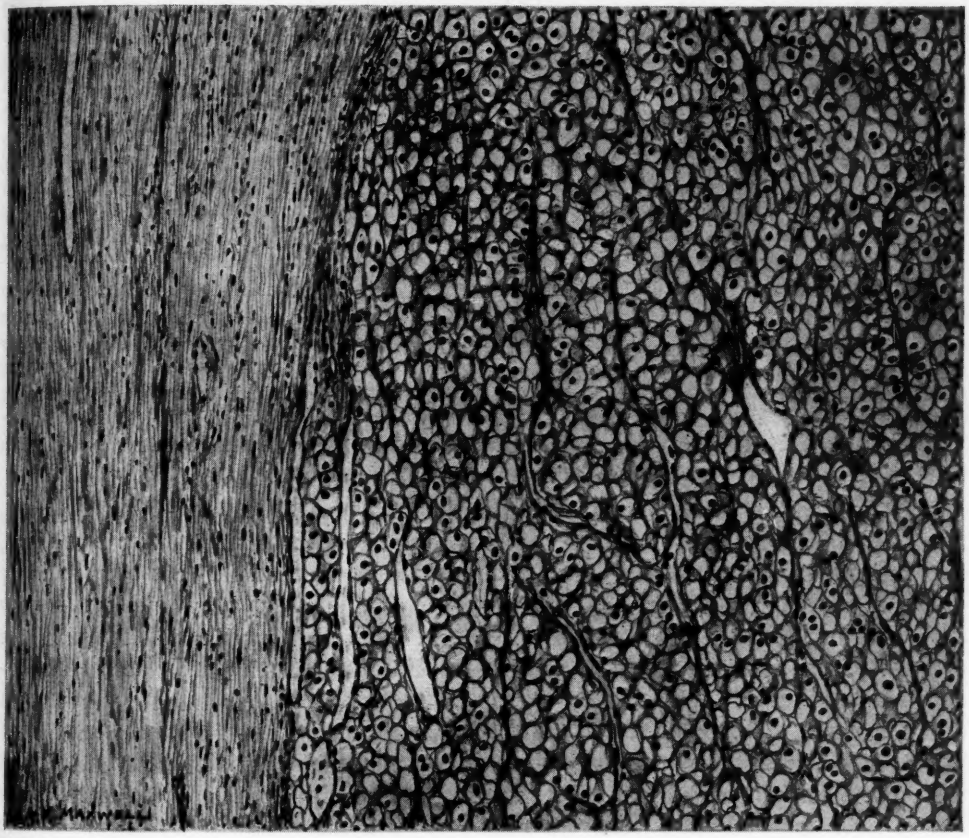

FIG. 190.—*Case* 2. A section of the secondary deposit in the cerebellum, showing the characteristic cells with clear cytoplasm and small darkly stained nuclei.

mobilized inwards and the kidney exposed. The renal vein was not infiltrated, but the kidney was very adherent, particularly at the upper pole. This was due to perirenal inflammation, as subsequent examination showed that the tumour occupied mainly the lower half of the kidney. At one stage it almost looked as if the operation would have to be abandoned, but eventually the tumour was removed whole. The patient was allowed out of bed three weeks later, but after making progress for a while, he took to bed again, as his gait was becoming more unsteady and pressure signs more evident.

PATHOLOGICAL REPORT (Dr. L. W. Proger).—Renal specimen. One-half of a right kidney which was removed by operation. It contains a lobulated tumour measuring 3 in. × 2¼ in., occupying mainly the lower half of the organ (*Fig.* 189, A). The lobules consist of pale yellow, solid masses separated from each other by fibrous strands. In one situation there are a number of thin-walled cysts containing clear or blood-stained coagulum; these are apparently

dilated tubules of the gland. The pelvis and upper calices are dilated and completely obstructed by a thick continuous layer of new growth springing from the inner surface.

Microscopical examination shows the growth to be a hypernephroma. It consists for the most part of relatively narrow elongated columns of large cells with clear swollen cytoplasm; in some places the cells are smaller and narrower with characters of ordinary columnar epithelium, with granular protoplasm. The connective tissue between the columns is scanty, and contains slit-like blood-spaces in places.

SECOND OPERATION.—Cerebellar decompression was performed on Sept. 4, 1933, and a well-defined tumour was felt on the under surface of the right cerebellar hemisphere. This enucleated easily. The blood-pressure was well maintained during the operation, but began to fall towards the end, and Cheyne-Stokes' respiration set in. Blood transfusion—one pint—was given, followed by intravenous saline. Shortly after the saline transfusion was begun, Cheyne-Stokes' respiration stopped abruptly. The patient's recovery from this second operation was much more rapid than from the first, and he was discharged from hospital on Oct. 8, 1933, walking well and with normal mental condition. His speech, which before operation had been thick and indistinct, regained its definition and precision. In the past five years his chest and osseous system have been periodically X-rayed for metastases, but so far all examinations have been negative. He has taken on extra work, and in a recent letter he states that his health continues to be excellent. Following his operation I suggested a course of X-ray therapy, but he was unwilling to undergo this. Consequently he has had no treatment of any kind since.

PATHOLOGICAL REPORT (Dr. L. W. Proger).—Cerebellar specimen (*Fig.* 189, B). An irregular globular tumour which was removed by a later operation from the same case as the hypernephroma of the kidney. It measured 1¼ in. in diameter and is enclosed in a thin layer of cerebellar tissue. The section shows it to consist of a firm pale yellow tissue with numerous small blood-vessels in the peripheral part; faintly yellow from degeneration but without actual softening. There is a well defined capsule around the growth. At one spot at the periphery considerable hæmorrhage has occurred. Microscopic examination shows the growth to have the typical structure of a hypernephroma (*Fig.* 190).

Comment.—These cases make an interesting contrast, in some respects alike, in others differing widely. In both there was an absence of urinary symptoms, and in both a metastasis first drew attention to the disease. There the similarity ends, for in one case a tumour which was not palpable infiltrated the kidney rapidly and caused widespread dissemination, while in the other case a slow, indolent type of growth gave rise to a solitary metastasis. An explanation for this striking difference is to be found in the pathology of these tumours, although it might be remarked that the views of pathologists vary greatly, not only with regard to the origin and nature of hypernephroma, but also with regard to the classification of renal cortical tumours. Some distinguish hypernephroma and several types of carcinoma, while others look upon all these tumours simply as malignant growths arising from one or other of the many different varieties of renal epithelium.

To distinguish the more malignant type of growth, Foulds and Braasch divide cortical tumours into alveolar carcinoma and adenocarcinoma. In alveolar carcinoma—the more malignant type—cellular differentiation is at a minimum, and there are in many instances solid cords, without lumens, of granular or clear cells, whereas in adenocarcinoma—the less malignant type—a high degree of cellular differentiation is present. According to these authors, some of the discrepancies noted in data concerning such tumours are due to a combination in the same tumour of adenocarcinoma and alveolar carcinoma.

The clinical history of the less malignant type is sometimes remarkably prolonged. With several of Israel's patients the histories dated back 20 years, and Kraft mentions a case where the history could be traced for 40 years. One of Ljunggren's patients had a palpable tumour for 30 years, and in Arkin's case, the

growth was known to have existed for 16 years. In the latter case, it was found at operation that the tumour was partly calcified and ossified, but in spite of this low grade of growth there was a recurrence locally shortly after operation. The slow rate of growth evidenced by these tumours seems to be imitated by their progeny, for cases have been recorded where secondary tumours have come to light long after the primary growth has been removed. Examples of such are the cases of Broster and Albrecht. Furthermore, and this is a consoling reflection for both patient and surgeon, such metastases not infrequently are solitary. Lehmann (quoted by Creevy) found that metastases were solitary in 13 out of 56 cases of metastatic hypernephromata as proved either at autopsy or by the prolonged survival of the patient. He recorded 34 additional cases in which metastases were solitary as shown clinically.

There is a point which has no concern with the subject matter of this paper, but to which I would like to make reference, and that is the history of head injury in the second case. In the discussion on head injuries at the Annual Meeting of the British Medical Association in 1933, Adams McConnell drew attention to some cases of his in which brain tumours had been associated with histories of head injury—the injury being purely incidental. He expressed the opinion that symptoms out of proportion to the severity and nature of the injury should arouse suspicion of the possibility of a tumour. Brain tumours, particularly cerebellar tumours, increase the risk of injury, and if the injury be a head one, it is a complication which might obscure the true diagnosis. In the case recorded here the head injury fortunately helped to accentuate the symptoms, and possibly that the gross hæmorrhage noted in the cerebellar tumour was due to this factor.

SUMMARY

1. It is not uncommon for hypernephromata to develop silently, and for metastases to be the first sign of the disease.

2. Metastases may cause confusion, and in the absence of a biopsy, investigation of the kidneys should not be forgotten.

3. Hypernephromata may be highly malignant, and cause widespread metastases. If the disease is to be forestalled, the slightest evidence of hæmaturia or renal pain is an indication for thorough urological investigation.

4. Hypernephromata, on the other hand, may be slow-growing, and dissemination may be confined to a solitary metastasis. Evidence of only one metastasis should encourage the surgeon to undertake the double operation, as it may mean complete eradication of the disease.

I wish to acknowledge my indebtedness to Dr. Gordon Holmes for his skill in localizing the cerebellar tumour; to Mr. G. T. Mullally, who, by his advice and help, contributed so largely to the successful removal of this tumour; and to Dr. L. W. Proger for the pathological reports of the two cases.

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RAISED INTRACRANIAL PRESSURE: HYDROCEPHALIC AND VASCULAR FACTORS*

By HUGH CAIRNS, Oxford

I propose to discuss some problems of raised intracranial pressure in the light of surgical experiences. In intracranial tumour there are at least four ways in which intracranial pressure can be increased: (1) By the growth in size of the tumour; (2) By œdema of the brain around the tumour; (3) By abnormal accumulations of cerebrospinal fluid in the cerebrospinal pathways; and (4) By increased bulk of blood in the capillaries and veins. It is of the last two of these that I wish to speak particularly.

At the outset certain premisses should be made clear. The rise of intracranial pressure occasioned by a tumour may be greater in the region of the tumour than in other parts of the cranial cavity. This is to a considerable extent explained by the presence of firm dural partitions, and in intracranial tumour herniations of brain tissue occur from one dural compartment to another (*Fig.* 191). But pressure is not always the same in all parts of one dural compartment. *Fig.* 192 shows an expansion of the skull produced by a dense fibrillary astrocytoma of the right temporal region. The expansion was limited to the temporal part of the right dural compartment, and thus we may conclude that the pressure was greater here than in the adjacent frontal and parietal regions.

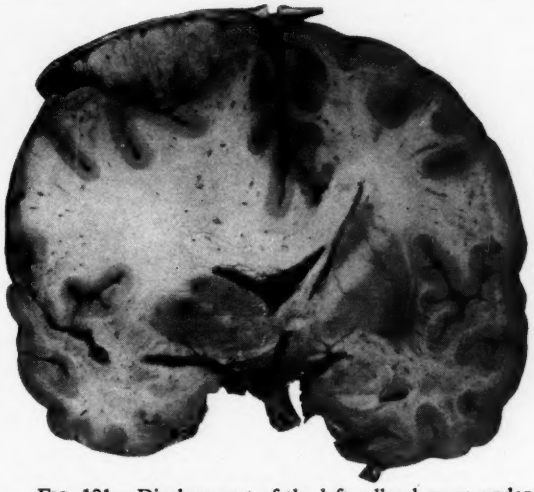


Fig. 191.—Displacement of the left callosal gyrus under the free edge of the falx cerebri in a case of left parietal meningioma. (No. 257.)

Of the factors responsible for differences of pressure in different parts of the same intracranial chamber, one must surely be the resistance of the arterial framework of the cerebral cortex; observations at operation indicate that arteries give way before pressure less readily than most other structures in the body. If in the course of its development a circumscribed tumour comes into relationship with cortical arteries, its expansion in certain directions must be limited by their unyielding quality. On the upper surface of the temporal lobe there is a barrier, some 3 cm. to 4 cm. wide, consisting of the main branches of the middle cerebral artery spread out like slings on the pial-glial membrane. In many temporal lobe tumours these vessels are stretched tight over the tumour.

The fact that intracranial pressure is not uniformly raised partly explains why a 'blind decompression', such as subtemporal decompression for an unlocalized

* A paper read at Cambridge on February 24, 1938.

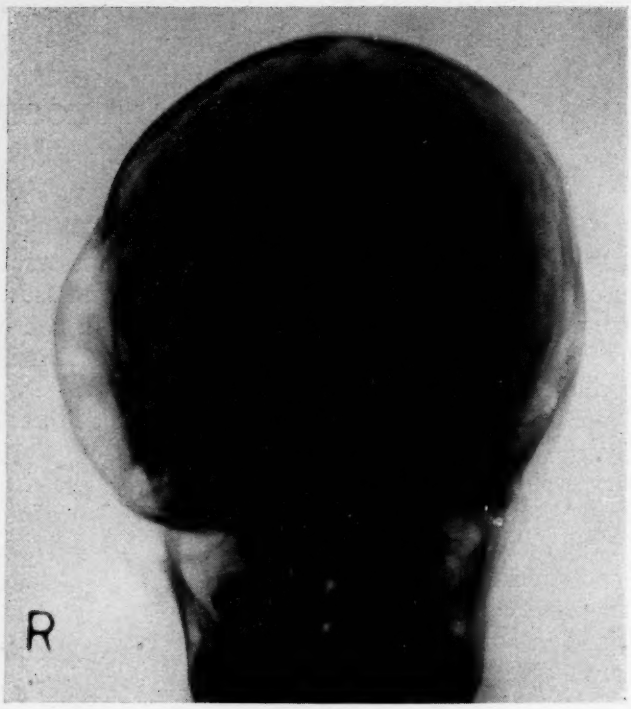


FIG. 192.—Bulging of the right squamous temporal bone due to an astrocytoma in the right temporal lobe in a child aged 7 years. The lateral ventricles are seen to be displaced to the left. (No. 1371.)

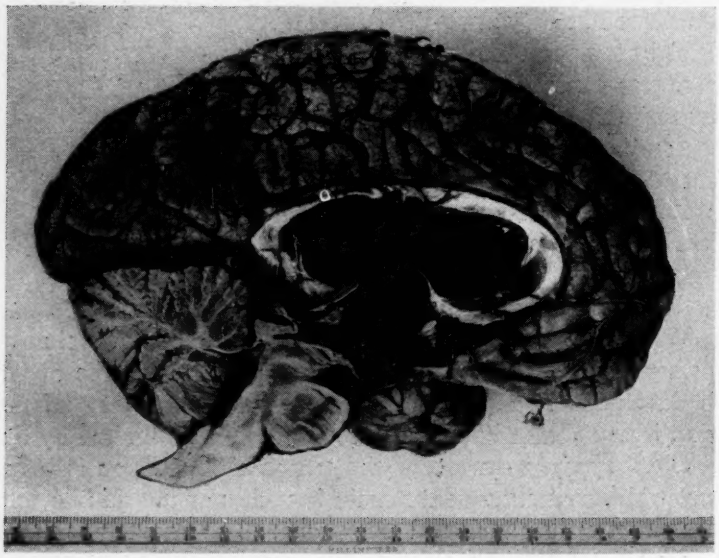


FIG. 193.—*Colloid cyst of the third ventricle.* Gross dilatation of the lateral ventricles with fenestration of the septum lucidum. In spite of the severity of the hydrocephalus the intraventricular pressure was less than 80 mm. H_2O. Behind the cyst the lateral ventricle bulges downwards, pushing the pineal gland before it. These structures are thus crowded into the tentorial opening. (No. 1658.)

intracranial tumour, is so rarely effective in relieving such symptoms as failure of vision from severe papillœdema. Experience has shown that operative decompression is only with certainty of value if it is done directly over the situation of the tumour. The best time for a palliative decompression is when the tumour has been exposed, and when the risks of the operation may be lessened by delaying its removal until a later stage.

Intracranial pressure as measured by lumbar or ventricular manometry is not invariably raised in expanding intracranial lesions. Some patients develop severe focal signs from intracranial tumour without ever showing a rise of the lumbar cerebrospinal pressure above the normal limit. This is especially the case with spongioblastoma multiforme in elderly people with shrunken brains. But such an observation does not mean that there is no rise of intracranial pressure around the tumour; nor does it necessarily mean that there is no general rise of pressure above the level that existed before the tumour began to grow. Low intracranial pressures are sometimes encountered also in cases of gross hydrocephalus which are the result of intermittent obstruction of the ventricular system (*Fig.* 193).

I. HYDROCEPHALUS

Hydrocephalus in intracranial tumour is sometimes a more complicated process than is generally supposed, for the growing tumour often produces obstruction at more than one point. This is best illustrated by tumours at the tentorial opening. The tentorial opening is the most vulnerable point in the cerebrospinal

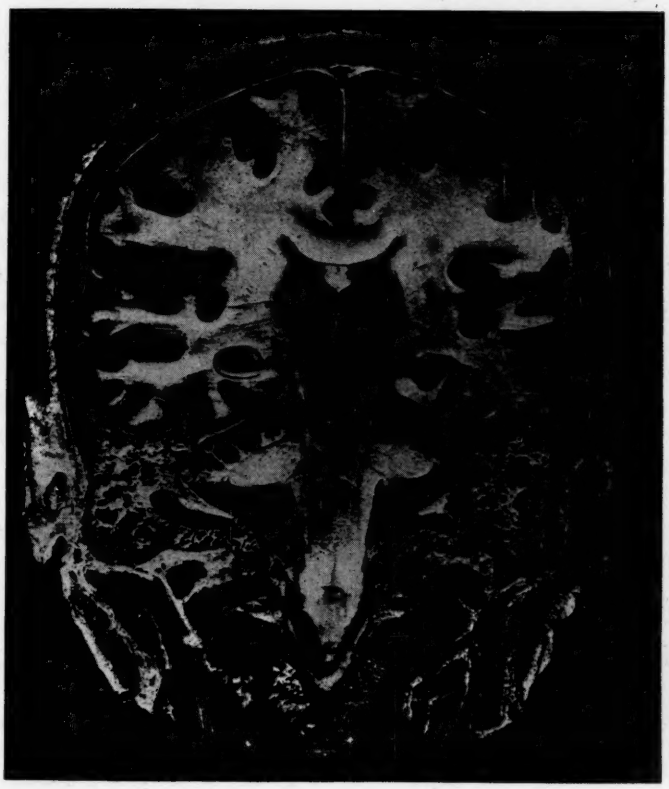


FIG. 194.—Coronal section of brain, showing the tentorial opening. (*From Macewen.*)

pathway, and acts as a bottle-neck both for the ventricular system and for the subarachnoid system (*Fig.* 194). All fluid passing downwards from the lateral

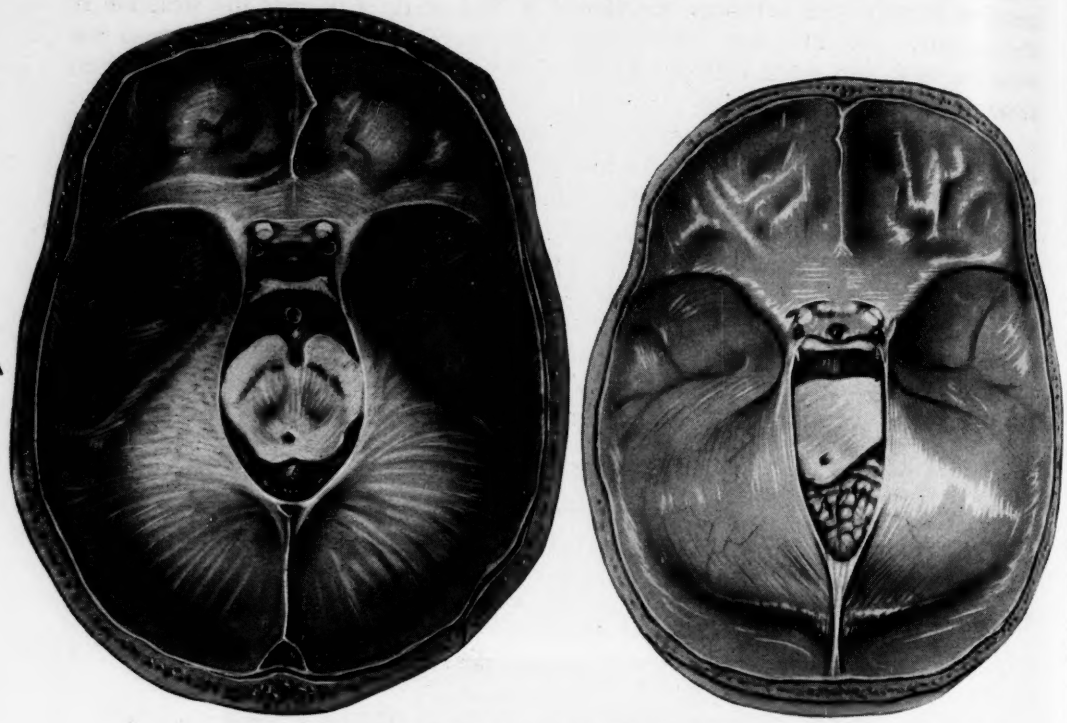


FIG. 195.—The tentorial opening from above. A, Normal (*from Penfield*). B, In a case of cerebellar abscess, showing obliteration of the subarachnoid cisterns of the brain-stem; in front the pons is flattened against the basi-occiput; behind, the vermis is displaced upwards through the tentorial opening. (No. 2413.)

FIG. 196.—Acoustic neurinoma embedded in the pons and adjacent cerebellum. (No. 1285.)

ventricles must pass through the aqueduct of Sylvius to gain exit from the brain, and all surface fluid passing upwards to be absorbed must effect a passage through the cisterns of the pons and midbrain at the bottle neck (*Fig.* 195, A). The free edge of the tentorium is a firm, almost unyielding structure. In view of these facts it is not surprising that a single lesion in this situation may obstruct both subarachnoid and ventricular channels.

Tentorial Obstruction from Below.—A good example of double obstruction at the tentorial level is provided by tumours of the cerebello-pontine angle. These tumours, for the most part acoustic neurinomas, are embedded in the ventrolateral aspect of the pons and cerebellum (*Fig.* 196).

As the tumour grows it displaces and narrows the aqueduct of Sylvius (*Fig.* 197), and gives rise to internal hydrocephalus. The tumour also occupies the greater part of the cistern of the cerebello-pontine angle. If this were all no serious obstruction of the subarachnoid space would occur, for the fluid could still travel upwards by the cisternæ of the other side. But as the tumour expands its upper pole may eventually push its way up to the tentorial opening and even through it (*Fig.* 198). The apex of the cerebellar vermis is pushed across to the opposite side and up into the cisterns around the vein of Galen, the pons is flattened against the basi-occiput, and thus the bottle-neck of the subarachnoid space is closed. A similar type of obstruction may occur in tumours of the cerebellar vermis and in abscess of the lateral cerebellar lobe (*Fig.* 195, B)—a lesion which is associated with severe œdema of the surrounding brain.

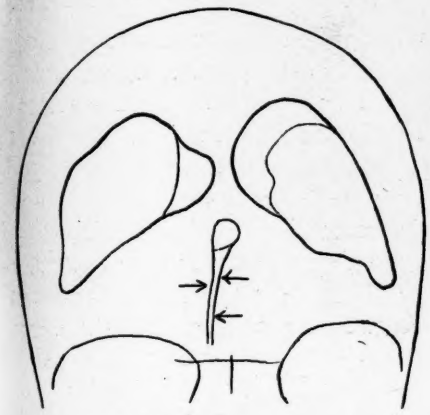


FIG. 197.—Displacement and narrowing of the aqueduct of Sylvius in acoustic neurinoma. The arrows point to the aqueduct. (*From Lysholm.*)

FIG. 198.—Meningioma of the cerebello-pontine angle extending through the tentorial opening into the interpeduncular space. (No. 557.)

Tentorial Obstruction from Above.—A tumour of one cerebral hemisphere usually tends to obliterate the homolateral ventricle, by its own bulk and by œdema of the brain around it. At the same time it causes dilatation of the lateral ventricle of the opposite side (*Fig.* 199), usually as a result of obstruction at the posterior part of the third ventricle or at the aqueduct of Sylvius, though sometimes the obstruction is farther forward.* In such tumours blockage of the subarachnoid space at the tentorial opening can occur as an additional obstruction. It is effected by displacement of the hippocampal gyrus over the edge of the tentorial opening and into the cisterns around the midbrain (*Fig.* 200); or, in medially placed temporal tumours, by extension of tumour itself in a similar direction (*Fig.* 201). Displacement of the hippocampal gyrus into the tentorial opening is most common in temporal

* I have seen a case of left frontal tumour in which at ventriculography the third ventricle was dilated, and at necropsy two days later, after an unsuccessful operation followed by hæmorrhage in the bed of the tumour, the third ventricle was completely obliterated. The site of maximum obstruction had changed.

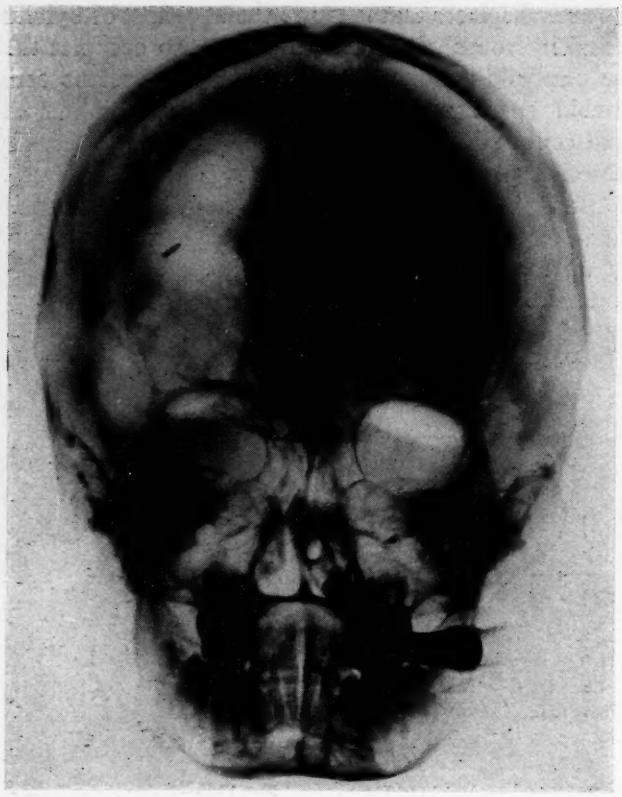
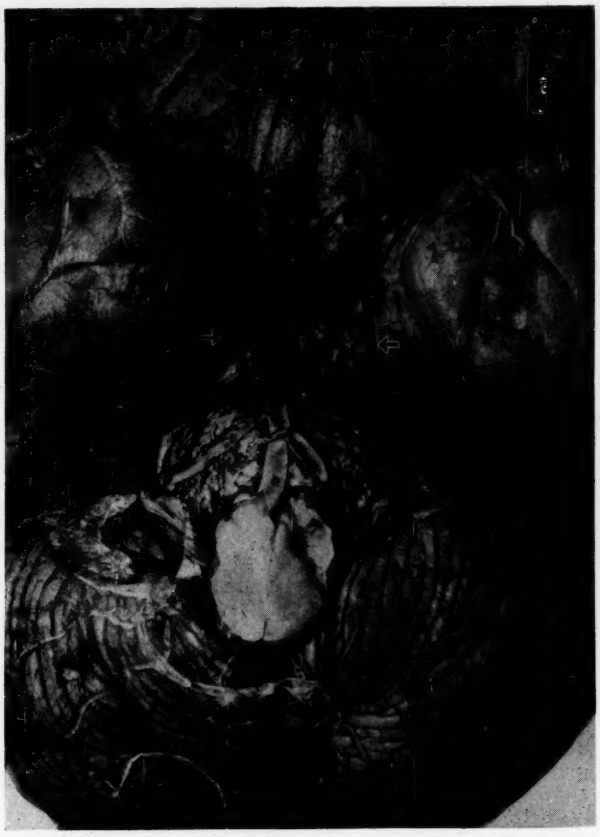


FIG. 199.—Dilatation of the right lateral ventricle in a case of a huge cystic and solid (partly calcified) ependymoma of the left cerebral hemisphere. (No. 3011.)

FIG. 200.—Herniation of the left hippocampal gyrus through the tentorial opening. The tentorial groove is marked with arrows.

FIG. 201.—A huge right temporal spongioblastoma multiforme which has spread through the tentorial opening into the right cerebello-pontine angle. (No. 254.)

A



B

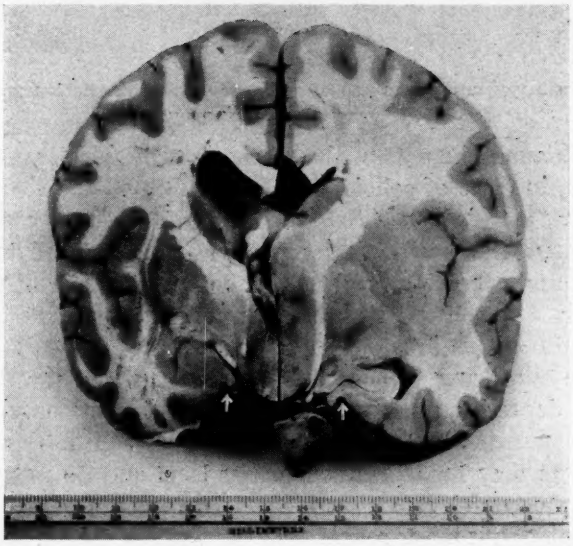


FIG. 202.—A, From a case of right frontal spongioblastoma multiforme. Herniation downwards of the hippocampal gyri is shown by the grooves (marked with arrows) on the inferior surface of each gyrus. These correspond to the free edge of the tentorium. More medially the third nerves can be seen, and each is marked with a groove corresponding to the petroclinoid ligament. (No. 218.) B, Tentorial grooves in the inferior surface of the hippocampal gyri, seen in coronal section (marked with arrows). From a case of unclassified granuloma of the third ventricle. (No. 1377.)

tumours, but it is also seen in tumours of other parts of the cerebral hemisphere, and in cases of bilateral hydrocephalus. In hemisphere tumours it is usually found also, in my experience, on the contralateral side, though less marked there than on the side of the lesion (*Fig.* 202). Associated with it there is downward displacement and compression of the third nerves against the edge of the petroclinoid ligament, and this is one of the causes of dilatation of the pupil, at first homolateral, then contralateral, a sign of impending disaster in expanding intracranial lesions. The herniated part of the hippocampal gyrus probably undergoes considerable swelling from interference with its blood-supply, if the patient lives long enough. Clovis Vincent and his pupils (1936) have described a group of symptoms in relation with this condition, and Vincent has called it the *temporal pressure cone*. Jefferson (1938) also has recorded his experiences of the displacement.

In advanced cases of symmetrical hydrocephalus the lateral ventricles may bulge through the tentorial opening, as in the case of colloid cyst illustrated above

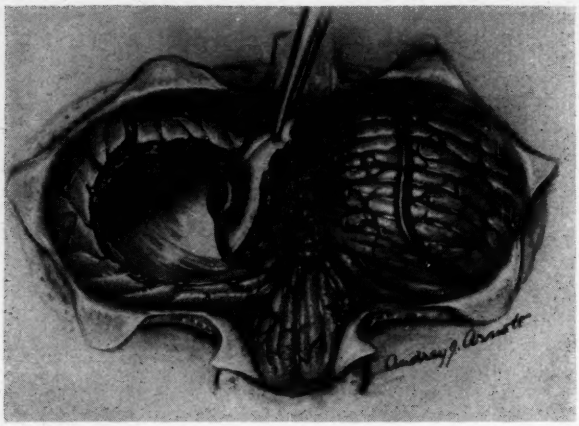


FIG. 203.—Cerebellar pressure cone in a case of cystic and solid hæmangeioblastoma of the left lateral cerebellar lobe. (No. 2494.)

(*see Fig.* 193). This may be part of the mechanism by which sudden death occurs, as it so often does, in cases of colloid cyst.

The Cerebellar Pressure Cone (*Tonsillar Herniation*).—In a considerable number of intracranial tumours the tonsils of the cerebellum are displaced downwards through the foramen magnum, even to a level below the lower border of the posterior arch of the axis. This displacement is most common in tumours of the cerebellum (*Fig.* 203), but it also occurs in supratentorial tumours (*Fig.* 204). In supratentorial tumours there are surprising variations in the incidence of the cerebellar pressure cone which may depend on normal variations in the anatomy of the cerebellar tonsils. In some normal subjects the tonsils project a little through the foramen magnum; in others they lie at a much higher level and do not project below the lower borders of the lateral cerebellar lobes. In tumours of the cerebello-pontine angle tonsillar herniation is never severe, and the cisterna magna is always capacious; these facts argue for the presence of *subarachnoid* obstruction at the tentorial level from a relatively early stage in the development of the tumour.

The symptoms associated with the cerebellar pressure cone include occipital pain, a stiff neck, and frequent vomiting; these may be the only prelude to sudden

death. In other cases dysarthria, drowsiness, short attacks of unconsciousness with extensor rigidity of the limbs and at times opisthotonos, diminution or absence of tendon-jerks, and the onset of bilateral pyramidal signs give additional warning of an impending catastrophe. Whether these symptoms are actually due to compression of the medulla oblongata by the herniated tonsils, or by some other mechanism, is not settled. From observations at operation there can be little doubt that the pressure cone does produce obstruction to the circulation of cerebrospinal fluid, with additional rise of intracranial pressure. The usual experience at operation in the presence of severe tonsillar herniation is as follows: On opening the dura the cerebellum bulges out under great tension. This pressure cannot be relieved by tapping, or even by aspirating, fluid from the lateral ventricles. The

FIG. 204.—Cerebellar pressure cone (A) in a case of glioma of the right parietal lobe (B). (No. 24.)

cisterna magna is completely occupied by cerebellum, and no fluid can be obtained from it. The pressure may be so high that there is risk of splitting of the surface of the cerebellum, with disastrous bleeding, and the only way to relieve it is to open the dura down to the lowest level of the tonsils, the posterior arch of the atlas, and if need be of the axis, having previously been removed. Fluid then gushes out under pressure and in considerable quantity, the whole cerebellum subsides, and the rise of pressure in the posterior fossa is now under control, though not completely relieved until the tumour is dealt with. Such evidence as I have is against the notion that the released fluid comes from the fourth ventricle, and the mechanism of fluid retention from tonsillar herniation is not clear.*

* From combined ventricular and spinal punctures Smyth and Henderson (1938) concluded that tonsillar herniation does not produce any difference between ventricular and spinal pressures, nor does it usually produce any obstruction to the downward passage of cerebrospinal fluid through the foramen magnum. This is at variance with the observations at operation that the pressure in the lateral ventricles may be reduced almost to zero and yet the pressure in the posterior fossa may remain extremely high.

Time will not permit me to describe in detail the other mechanisms whereby tumours produce obstruction of the cerebrospinal pathways at multiple points, but a few of them may be briefly mentioned. In tumours of one cerebral hemisphere the subarachnoid cistern of the great longitudinal fissure may become blocked by extension of tumour, or by displacement of an œdematous callosal gyrus beneath the free edge of the falx. The cisterna chiasmaticus may be blocked by displacement of the posterior edge of the gyrus rectus into the anterior angle of the optic chiasm. And the cisterns of the Sylvian fissures may become partially filled by displacement of the posterior part of the inferior surface of each frontal lobe. In addition, all basal tumours appear to cause obstruction in the cisterns around them. A systematic description of these displacements has been given by Spatz and and Stroescu (1934).

TREATMENT OF THE HYDROCEPHALUS OF INTRACRANIAL TUMOUR

When we come to consider operative treatment of tumours in the light of these observations, it is important to bear in mind that more than one of these several mechanisms may come into play in any one case of intracranial tumour, the more so in cases of slowly growing benign tumours that distort the brain so gradually as to produce very few symptoms until great displacement has occurred. These benign tumours are usually cases in which operation can produce very good results, but surgical measures will be unsuccessful unless the manifold character of the hydrocephalic factors is gauged with a fair degree of accuracy. This may be illustrated by consideration of three varieties of tumour—acoustic neurinoma, temporal glioma, and meningioma of the lesser wing of the sphenoid.

Acoustic Neurinoma.—Patients with acoustic neurinoma usually seek treatment because of headache and the effects of papillœdema, or because of cerebellar ataxia. Experience has shown that by cerebellar decompression, with or without partial intracapsular enucleation of the tumour, the patient can usually be relieved of headache and papillœdema, but his ataxia is not lessened and may even be increased. The area of decompression may become expanded to an enormous extent (*Fig.* 205). Commenting on the results of intracapsular enucleation of acoustic tumour, so great an authority as Cushing (1930) said, " In the average case, if the pressure effects of the tumour can be so far overcome by an intracapsular excavation as to permit a subsidence of the choked disc and thus to save vision, one may well be content ". Incomplete intracapsular removal of the tumour has the effect of releasing the aqueduct obstruction, but it rarely relieves the obstruction of the subarachnoid space at the tentorial opening. This can only be effected by thorough removal of the upper pole of the tumour, and dislodgement of the vermis from the tentorial opening.

Temporal Tumours.—In most temporal tumours it is not necessary to deal directly with the herniated hippocampal gyrus, but in those cases where intracranial pressure is greatly raised, as indicated by high papillœdema, repeated attacks of headache and vomiting, drowsiness, and oculomotor palsies, it is advisable to do more than remove the tumour to ensure survival of the patient. After the tumour has been removed the surgeon should gently dislodge the temporal lobe from the upper surface of the tentorium until cerebrospinal fluid flows freely from the region

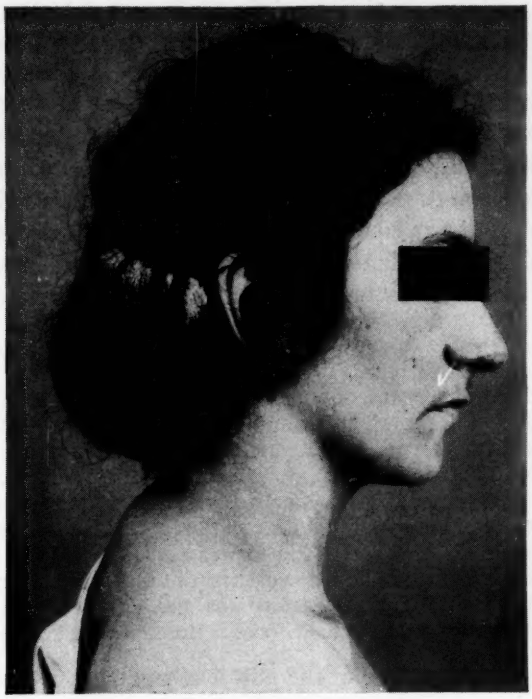


FIG. 205.—Bulging of the cerebellar decompression in a case of acoustic neurinoma treated elsewhere by simple decompression. The enormous size of the decompression shows that there is still obstruction in the subarachnoid cisterns at the tentorial opening. (No. 1363.)

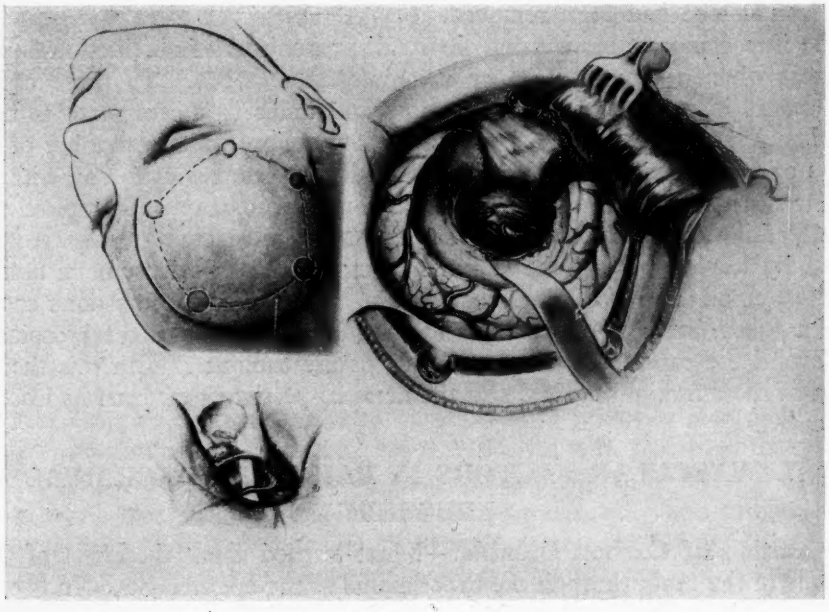


FIG. 206.—Meningioma of the right lesser wing of the sphenoid. Part of the frontal lobe has been resected to expose the tumour. The insert shows the site of attachment of the tumour to the dura of the base of the anterior clinoid process. (No. 1571.)

of the tentorial opening. If this step proves impossible the deeper part of the temporal lobe should be removed, as recommended by Clovis Vincent, until a free flow of fluid from beneath it indicates that tentorial obstruction of the subarachnoid space has been relieved.

Sphenoidal-ridge Meningioma.—A flow of cerebrospinal fluid from the depths of the wound is one of the most welcome signs that a surgeon can see during removal of an intracranial tumour. Not only does it indicate relief of hydrocephalus, but there is also relief of tension and of venous oozing in the operative field, and the remaining steps of the operation are much easier. The following case is an interesting example of local subarachnoid hydrocephalus in a meningioma of the lesser wing of the sphenoid.

The patient was a female, aged 50, with bilateral papillœdema (2 D.) and secondary optic atrophy, and a lumbar pressure of 240 mm. H_2O. At operation under easy intratracheal gas and oxygen anæsthesia the right frontal lobe was exposed. It was pale and very tight, and the tension was not appreciably relieved by 60 c.c. of 15 per cent NaCl intravenously. A piece of the frontal lobe was resected to gain exposure, and the tumour (which was no more than 3·5 cm. in diameter) was then removed piecemeal (*Fig.* 206). After more than half of its substance had been so removed, the remainder of the tumour was gradually dislodged from its bed and tilted forwards. The Sylvian fissure had previously been opened and been found dry. But now, when the tumour was tilted forwards, cerebrospinal fluid gushed from the cisterna chiasmaticus and interpeduncularis in large amounts, and the tension of the whole operative field was for the first time reduced.

This is a remarkable example of the power of tumours, even quite small tumours, to obstruct the subarachnoid spaces. The effect of such obstruction upon the the intracranial contents as a whole is even more remarkable: in this case the fluid pent up in the basal cisterns produced such rise of tension that the whole right frontal lobe bulged tightly, and it was not possible to expose the tumour until part of the frontal lobe had been removed.

The importance of recognizing the dual mechanisms of obstruction is particularly great when a tumour is to be incompletely removed. To those concerned with tumours in various parts of the trunk and limbs it is repugnant to think of incomplete removal of tumours, but within the cranium quite a number of benign tumours of long standing are best treated by incomplete removal, and with lasting benefit to the patient. The acoustic neurinoma is an example: complete excision is usually followed by facial palsy, and the most satisfactory results are usually obtained by leaving part of the capsule, together with a little tumour tissue. In such cases, among the indications that tell the surgeon that he has done enough to achieve a good functional result, not the least is a free flow of cerebrospinal fluid from beyond the capsule of the upper pole of the tumour. With this the vermis falls out of the tentorial opening, and the dreaded persistent external hydrocephalus is prevented.

II. VASCULAR FACTORS IN RAISED INTRACRANIAL PRESSURE

Inhalation of Carbon Dioxide.—I first learned about the effect of CO_2 on the vessels of the brain through the experiments of my anæsthetists. In two operations I was able to observe the effect of inhalation of CO_2 upon the exposed brain. The percentage of CO_2 given was not accurately measured because of rebreathing, but was probably in the region of 10 per cent.

The first patient was a man of 25 (No. 1372) with a high vermis astrocytoma. The operation was performed under intratracheal ether-gas and oxygen, and the initial pressure in the right lateral ventricle was 600 mm. of water. When the dura was opened the cerebellum bulged out a little, but not excessively. Suddenly, however, the whole cerebellum swelled, its surface vessels became greatly dilated, the cerebellar cortex split, and blood started to pour from many points. Subsequently I discovered that, unknown to me, the anæsthetist, who was not accustomed to giving anæsthetics for intracranial operations, had given CO_2 mixture to increase respiratory excursion because the patient showed a tendency to vomit as the dura was being opened. There was no rise of arterial pressure during the period of brain swelling, or at any other time during the operation. This patient died after operation, and at necropsy no hæmorrhage was found within or about the

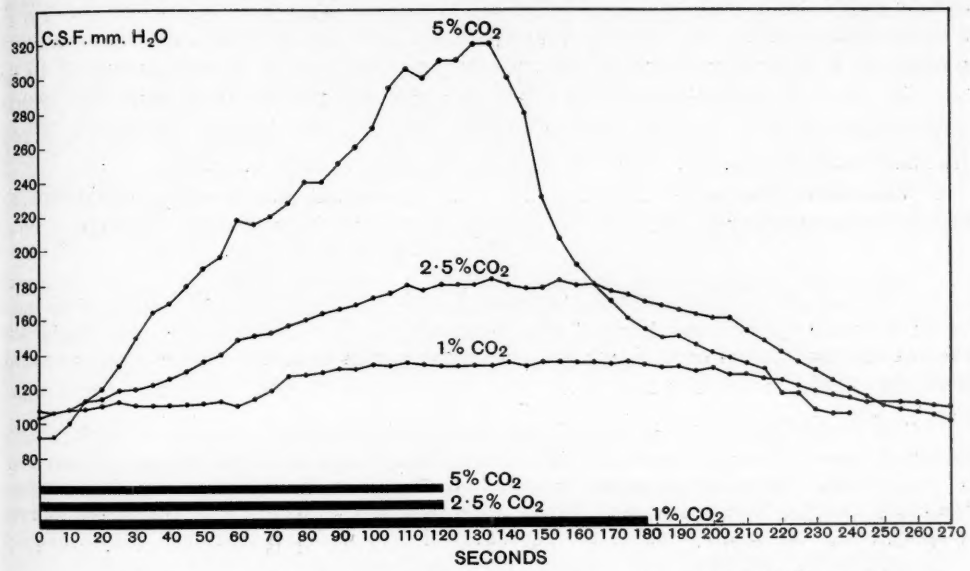


FIG. 207.—The effect of inhalation of carbon-dioxide–oxygen mixture on intracranial pressure, as measured by spinal manometry.

astrocytoma to account for the sudden rise of intracranial pressure during operation.

In the second case, a girl aged 16 (No. 2711) was being operated on for a cerebellar tumour under intratracheal gas and oxygen (initial ventricular pressure, 450 mm.). The cerebellum bulged out strongly when the dura was opened, but a cyst was found in the lower part of the vermis and left cerebellar lobe, and after it was emptied the severe rise of tension in the posterior fossa was relieved. Meanwhile the intratracheal tube had become blocked with mucus so that it had to be removed. To stimulate breathing when attempting to re-introduce the tube the anæsthetist gave CO_2 through an intrapharyngeal tube. The sudden swelling of the cerebellum and its vessels was so strongly reminiscent of the previous case, that it was possible to accuse the anæsthetist of administering CO_2 without having been previously aware of the nature of his activities. Fortunately at this time the high intracranial tension had already been relieved, and the CO_2 was stopped before any serious damage was done.

Subsequently we tried the effect of CO_2 inhalation upon intracranial pressure as measured by spinal manometry. *Fig.* 207 shows a typical result. The carbon dioxide, mixed with oxygen, was given through a mask without producing any venous engorgement of the face or neck. As *Fig.* 207 shows, even concentrations of CO_2 as low as 1 per cent will produce a rise on intracranial pressure; with 5 per cent CO_2 the pressure may rise more than 200 mm. H_2O in less than 2 minutes' inhalation. Nitrous-oxide inhalation and simple hyperpnœa produce no rise of pressure. Similar observations have been made by Cobb and Fremont Smith (1931).

Much work has been done by Bronk and Gessell (1934), Gibbs, Gibbs, and Lennox (1935), Wolff (1936), and others to show that CO_2 has a powerful vasodilator effect upon the vessels of the brain, and Schmidt and Pierson (1934) have shown that the CO_2 acts directly upon the vessel walls. The surgical experiences reported in this paper show that the effect is no less in man than in the lower animals, as was already indicated by the work of Gibbs, Gibbs, and Lennox, and that it is accompanied by a rise of intracranial pressure proportional to the concentration of CO_2.

In cases of raised intracranial pressure there are certain phenomena for which explanation must be sought, it seems to me, in some mechanism similar to, if not identical with that of the direct action of CO_2 on the cerebral vessels.

Vascular Factors.—The way in which vascular factors may contribute to rise of intracranial pressure may be illustrated by two cases of cystic glioma.

Case 1 (No. 2005).—In the first case, through a small burr hole, 75 c.c. of fluid was aspirated from a cystic glioma of the left temporal lobe, under an initial pressure of 60 mm. of cystic fluid. No air was injected, but a radiograph taken immediately after aspiration showed that air had got in alongside or through the needle to take the place of the aspirated fluid (*Fig.* 208).

Case 2 (No. 1313).—In the second case, through a small burr hole, 50 c.c. of fluid were aspirated from a cystic glioma of the right frontal lobe, under an initial pressure of 200 mm. of cystic fluid. A radiograph taken immediately afterwards showed that no air had got into the cystic cavity. The patient died fifteen hours later and at necropsy he was found to have a spongioblastoma multiforme of the right frontal lobe and the cyst was quite collapsed (*Fig.* 209).

What is the explanation of the difference of response to reduction of the intracranial content in these two cases? In the second case at necropsy there was no evidence of hæmorrhage into the cyst or into the tumour (*Fig.* 209), and there was no large collection of cerebrospinal fluid, in the ventricles or elsewhere, to take the place of the cystic fluid. In these circumstances it is only possible to assume that the 50 c.c. of space created by withdrawal of cystic fluid from the intracranial chamber was immediately taken up by dilatation of blood-vessels. Let us contrast the clinical states of the two cases.

Case 1.—Male, aged 46 (No. 2005). For five weeks he had suffered from lassitude and drowsiness, followed by pain in left eye and cheek, increasing disturbance of speech, and for one week increasing weakness of the right side. The following physical signs were observed: blurring of the optic discs, complete right homonymous hemianopia, gross sensory loss of all forms, and severe weakness of the right arm and leg. Blood-pressure, 155/100 mm. Hg. Pulse rate, 60. Lumbar puncture: initial pressure, 250 mm. H_2O; protein content of cerebrospinal fluid, 0·1 per cent.

On the day of aspiration the patient became worse. For the first time he had a severe headache, his pulse became slower, and he vomited once. At the time of operation he was

FIG. 208.—*Case* 1. Radiograph taken immediately after aspiration of the cystic fluid, showing air in the cyst. (No. 2005.)

A B

FIG. 209.—*Case* 2. A, B, Spongioblastoma multiforme of the right frontal lobe. A cyst containing 50 c.c. of fluid was aspirated shortly before death. The collapsed cavity of the cyst can just be discerned on the medial aspect of the solid tumour in A. (No. 1313.)

rapidly becoming stuporous. After aspiration of the cyst he was greatly improved, but symptoms recurred, and he died one month later. The tumour is shown in *Fig.* 210.

FIG. 210.—*Case* 1. Cystic and solid spongioblastoma multiforme. (No. 2005.)

Case 2.—A male, aged 30 (No. 1313). He had suffered from epileptic seizures for one year. For two months he had felt tired and weak, and for one month had had attacks of headache and vomiting of increasing severity. One week before admission to hospital he became delirious and incontinent. On examination he showed slight bilateral papillœdema; his pupils were small, irregular, and fixed to light; there was bilateral ptosis, diminution of upward movement of both eyes, slight lower facial weakness on the left side, and both knee-jerks were exaggerated.

Next morning he became unconscious. Both his pupils became large and irregular, and still failed to react to light. His corneal reflexes were absent and his knee-jerks could no longer be obtained. He was given 70 c.c. of 15 per cent NaCl and within twenty minutes responded to pin, moved his arms and throat a little, and his corneal reflexes returned. One hour later, however, his condition was as bad again as it had been before, and it was decided to tap the right frontal lobe, though most of those who had seen him thought he had a midbrain tumour. At the time of operation, about six hours after the first onset of deep coma, he was deeply unconscious and blue; his blood-pressure, now taken for the first time, was 190/100 mm. Hg; his pulse-rate was 84, but rose to 140 when the operation was begun under novocain anæsthesia, although there was virtually no loss of blood.

After the cyst had been tapped his colour improved and he became restless. His pulse rate dropped to 110, but quickly returned to 140; the blood-pressure dropped to 170/70 mm. He did not regain consciousness and died fifteen hours later. At necropsy, in addition to the tumour (*see Fig.* 209), there was considerable œdema of the brain around the tumour, engorgement of all the cerebral veins, displacement of the right gyrus rectus backwards against the optic chiasm, a severe cerebellar pressure cone, signs of pressure on both third nerves, and a small hæmorrhage in the midbrain in the region of the right third nerve nucleus.

Comment.—Thus, in the first case stupor was of recent onset, arterial blood-pressure was within normal limits, and there was no ophthalmoplegia; in the second case stupor was of some days' duration and associated with ophthalmoplegia, and before operation the patient had become comatose and his arterial blood-pressure had reached a high level. In the first case the rise of intracranial pressure was readily compensated for by removal of 75 c.c. of cystic fluid, so much so that air

rushed in to take the place of some of the fluid. In the second case removal of 50 c.c. of fluid was insufficient to relieve the rise of intracranial pressure; no air rushed in through the needle and all the space gained was occupied at once by the intracranial vascular bed.

Of the vascular factors in raised intracranial pressure the best known is the rise of arterial pressure in acute cerebral compression. As Cushing (1901) showed experimentally many years ago, when the intracranial pressure is rapidly raised up to or beyond the level of arterial pressure, there is a compensatory rise of arterial blood-pressure, due to activity of the vasomotor centre. This mechanism is often seen in such acute rises of intracranial pressure as extradural hæmorrhage and acute subdural hæmatoma. It was probably present also in *Case* 2, though there is no proof that the dilatation of blood-vessels, which must have taken place after the cyst was emptied, was directly due to the rise of arterial pressure. Indeed, the experimental work suggests that rise of arterial blood-pressure is not an essential factor in dilatation of the cerebral vessels.

The number of cases of raised intracranial pressure in which the arterial pressure is also raised is small; they are mostly cases of massive intracranial hæmorrhage from trauma or from cerebral vascular disease. It seems that if intracranial pressure is raised slowly the arterial blood-pressure does not alter.

FIG. 211.—Dilated emissary veins at the external occipital protuberance. From a case of stricture of the aqueduct of Sylvius. (R. 1984.)

Most cases of intracranial tumour have a low arterial blood-pressure, as was pointed out some years ago by Russell Brain (1925). There is a good deal of evidence, however, that in chronically raised intracranial pressure the venous pressure is raised. In most cases of tumour with a long history of illness and high papillœdema radiographs show abnormally large openings and channels for emissary veins in the region of the external occipital protuberance (*Fig.* 211). In children with chronically raised intracranial pressure large sinusoidal vessels can sometimes be felt in the scalp over the posterior part of the sagittal sinus, and these veins, for such they are shown to be at operation, may give a loud systolic murmur.

In operation for cerebellar tumours, unaccompanied by rise of arterial pressure, it is a common experience at operation under general or local anæsthesia to encounter severe venous bleeding from the emissary veins of the torcular region, and indeed from all the veins. And it is found also that the venous pressure can be lowered and the bleeding appreciably diminished by withdrawing cerebrospinal fluid from the lateral ventricles. Reduction of intracranial pressure by this method is indeed a routine method of diminishing venous bleeding in the early stages of cranial operations. Pressures encountered in the ventricles often measure as high as 600 mm. of H_2O, and occasionally 900 mm. The cerebral veins must have a slightly higher pressure than the cerebrospinal fluid, or they would collapse; that is to say, often a pressure of 50 mm. of Hg is demanded in them, and even on occasions 70 mm. of Hg. Just how this rise of venous pressure is brought about is, so far as I am aware, not yet explained. It is not difficult to believe that in the presence of alterations of cerebral bulk and dislocation of the hemispheres a few cerebral veins are obstructed by the tumour, and that the remainder can be kinked at the place where they pierce the arachnoid to enter the sagittal and other venous sinuses, by displacement of the brain owing to rise of pressure, as has been suggested by Wright (1938). But the evidence at operation, and also by radiography, is that there is also rise of pressure in the torcular emissary vessels, and these come directly from the great venous sinuses.

Acute Brain Swelling.—There is a dreaded though fortunately rare complication of operation for removal of intracranial tumours in which the whole of the brain that is unprotected by intact dura swells, and swells to such an extent that it is impossible to replace the osteoplastic flap, and the skin wound can only be sutured with difficulty. The appearance is identical with that seen after the inhalation of CO_2. This swelling may occur without massive deep-seated hæmorrhage as its underlying cause, and without any rise of arterial blood-pressure. From the manner in which blood-vessels in the swelling brain start to ooze there is clearly a great rise of venous and capillary pressure. Resection of the swollen area is attended by disproportionate bleeding. The following case is an example.

Case 3. **Melanotic carcinoma of left frontal lobe. Operation. Acute brain swelling. Death.**—A woman, aged 46 (No. 2123) had suffered from fatigue, loss of interest, and headache for a period of six months, and for two weeks had become increasingly drowsy and listless. Examination showed severe bilateral papillœdema (5·5 D.), absence of tendon-jerks except the ankle-jerks (which were diminished), a slow pulse, 40–60, slight bilateral external rectus weakness, and slight weakness of right lower face and of right upper limb.

At consultation it was considered that the evidence of localization was insufficient and that ventriculography should be done. The left ventricle could not be found; from the

right 2 c.c. of fluid escaped with great force, before its pressure could be measured. Air was introduced very slowly while fluid escaped drop by drop. The radiographs indicated a left hemisphere tumour.

At operation, which was undertaken immediately after the X-ray examination, the dural veins and sinuses bled severely and the dura was stony hard, even though the right ventricle was being drained by an indwelling needle at the time. When the dura was opened the cerebral veins were seen to be greatly engorged. A film of blood began to spread under the pia-arachnoid from the region of the left Sylvian fissure. A circumscribed frontal tumour was found, and, as in most cases of metastatic tumour, was easily removed, with the minimum injury to the surrounding brain, which was soft and œdematous. At this stage the brain began to swell. The bed of the tumour became rapidly obliterated and blood began to ooze from many points. Every interference gave rise to more bleeding. A fragment of muscle was put in the tumour bed, the bone-flap was sacrificed, and the skin closed. The patient died two hours later. Sections of the tumour showed it to be a secondary melanotic carcinoma. There was no necropsy. During operation the highest blood-pressure was 140/90, and the pulse-rate rose from 70 to 120.

Acute brain swelling is usually fatal, though not invariably so. In the case just described intracranial pressure was extremely high before any intervention, and was aggravated by ventriculography. In other cases I have seen brain swelling come on after severe and prolonged traction of the brain over a deep-seated tumour, and there is no doubt that in such cases it is encouraged by too wide an opening of the dura. Histologically the swollen brain shows very great dilatation of all its capillaries and small venules, and multiple small areas of hæmorrhage about these vessels. It is this dilatation of the vascular bed which must be responsible for the brain swelling. The cause of the swelling of the vascular bed in acute brain swelling and of the raised venous pressure in chronically raised intracranial pressure constitute an important problem in intracranial pathology. The resemblance of the changes to those produced by inhalation of CO_2 suggests that at some stage, whether from slowing of the circulation of blood in the brain or from some other cause, the CO_2 tension is raised with the precipitation of brain swelling.

SUMMARY

The hydrocephalic and vascular factors that contribute to raised intracranial pressure are discussed. In expanding intracranial lesions the rise of intracranial pressure is not uniform, even in a single dural compartment. Displacements of brain tissue occur, and may block the subarachnoid space; and thus hydrocephalus in intracranial tumour may often be the result of obstruction of the cerebrospinal pathways at more than one site: the ventricular channels are blocked, and the subarachnoid cisterns may also be blocked. This fact has important bearings on the operative treatment of tumours.

The vascular factors of raised intracranial pressure include: (1) A rise of arterial pressure which occurs only in acute and severe cerebral compression; and (2) A rise of cerebral venous pressure, and presumably capillary pressure, in all cases of raised intracranial pressure. This second factor is probably responsible for acute brain swelling, the clinical and pathological pictures of which are described. The changes produced on the human brain by inhalation of low concentrations of carbon dioxide are described, and the significance of their resemblance to acute brain swelling is discussed.

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CONGENITAL DIVERTICULUM OF THE COMMON BILE-DUCT

By Sir JAMES WALTON, London

Congenital diverticulum, or congenital cystic dilatation of the common bile-duct, has long been recognized as a very rare lesion. Nearly all the contributions to the literature are based on the experience of a single case, a careful search failing to reveal an example of any author who has reported more than two cases. Judd and Greene in 1928 stated that their case was the sole example occurring at the Mayo Clinic in a series of 17,381 operations upon the biliary tract. Waller states that Langenbach in 1897 was able to find only one reported case, that of Konitzky. In 1909 Ebner collected 11 cases, but in the same year Lavenson had increased this number to 29. Waller's comprehensive monograph in 1917 discussed 35 cases, including one of his own, and gave an abstract of every case that had been published up to that time. In 1928 Willis was able to collect 60 reported cases. Although so rare a condition, many valuable articles have been published upon it, the most complete being those of Waller, Morley, McWhorter, Judd and Greene, Wright, Saint, and Zinninger and Cash, upon whose works I have drawn very fully. Most of these reports contain a full review of the literature, but it is possible that many articles were overlooked owing to the ambiguity of their titles. A case, for instance, reported by Burman in 1912 as a huge dilatation of the common bile-duct appears to be a true example of the disease, although it is not included in Waller's list. With an increasing number of reported cases, discrepancies are beginning to appear in the totals: thus Wilson, writing in 1930, included 93 cases, but Zinninger two years later would accept only 82. It would therefore seem that but little is to be gained by attempting to collect all the reported cases.

An unusual personal experience of five clinical cases stimulated a fresh examination of the subject, and an attempt to discover whether its rarity was real or only apparent and due to many cases being overlooked. My own five cases occurred in a series of 1178 operations upon the biliary tract, and the condition therefore appeared to be more common than is usually stated. An investigation of the London Hospital statistics showed, however, that this was not the case. Of the 5 clinical examples, 3 occurred in hospital practice. During the twenty-six years 1913–38 inclusive, there were admitted 415,626 patients, of whom 246,552 were classified as surgical cases. In the pre-operative and operative diagnosis there was only one instance of diverticulum of the common bile-duct, which was my own first case; but the fourth and fifth cases were operated upon within a week of each other, and occurred in January, 1939, among a total of approximately 1000 admissions. I am also informed that none of my surgical colleagues at this institution have met with a single example.

It was possible, however, that cases have been overlooked, and therefore the post-mortem records were investigated. It was found that in the thirty-two years

1907–38 inclusive, there had been at the London Hospital 23,048 post-mortems, among which there had been only 2 examples of this condition, one of which was my own first case, the other being *Case* 6 here recorded. There was one other example (P.M. 285, 1934) which was regarded as doubtful in that there was considerable dilatation of the common duct without any visible obstruction; but as the dilatation was only moderate (8 cm. circumference), involved the whole duct and the hepatic ducts, was uniform and not saccular, and occurred in a woman of 55 years of age, it was regarded as belonging to a different category and was not included.

There can, therefore, from these figures be no doubt that the lesion is one of extreme rarity.

CASE REPORTS

Clinical Cases

Case 1.—B. D., a young girl aged 16, was seen at hospital on Jan. 1, 1926. Five weeks before she had been admitted on the medical side under Dr. Hutchison. She had complained of nothing herself, but her mother had noticed that her abdomen had been enlarging for some weeks, and that she was getting rather pale. Her menstrual periods had commenced two years before, but had been getting less and had almost entirely ceased for about 9 months. Friends and relatives had accused her of being pregnant, and for this reason her mother sought advice. The patient stated that she had no pain, she had never vomited, and she did not know that her abdomen was large. She had never been jaundiced. There was no past history of any illness.

On Examination.—She was a rather poorly developed girl with considerable anæmia. The abdomen was enormously distended, with a fluid thrill and shifting dullness. There was no œdema of the legs. The heart and lungs were clear. The patient was kept at complete rest in bed with a course of iodide of iron and cod-liver oil. The ascites diminished and a greatly enlarged spleen was then palpable. It reached about 2 in. below the umbilicus. The liver was not palpable and no tumour could be felt. The Wassermann reaction was negative. The blood showed a secondary anæmia: red blood-corpuscles 3,400,000, hæmoglobin 45, colour index 66. The differential white count was normal and there was no leucocytosis. The condition was regarded as an advanced case of splenic anæmia, and I was asked to see her, and I agreed that a splenectomy might be helpful in retarding the progress of the disease.

Operation (Jan. 3, 1926).—The abdomen was opened by an upper right paramedian incision, and much fluid escaped. The spleen was greatly enlarged, with considerably dilated vessels, and it was removed. After removal a large cystic swelling, about the size of a coco-nut, was found at the lower end of the common bile-duct; the liver was rather smaller than normal and was a little nodular and irregular; the gall-bladder was very slightly dilated. A hypodermic needle withdrew some thin bile from the cyst, over which the duodenum was stretched on its lower and inner aspects. An anastomosis was performed between it and the cyst, and the wound closed. The next day the patient collapsed and died.

Post-mortem Examination.—Thrombosis of portal, splenic, and superior mesenteric veins. Cirrhosis of liver. Enormous dilatation of bile-ducts, commencing 3 cm. above ampulla of Vater. The dilatation formed an almost spherical cyst 9 cm. in diameter (*Fig.* 212) with a thick dense wall $\frac{1}{3}$ cm. thick. Mucosa bile stained with many large shallow ulcers. Active opening between anterior surface of cyst and duodenum 6 cm. beyond pylorus. Great dilatation and thickening of both hepatic ducts, moderate dilatation of cystic duct, and slight dilatation of gall-bladder. All these ducts opened into the cyst by constricted orifices. No dilatation of intrahepatic ducts. Lower portion of common duct opened obliquely at a very acute angle into the dilated sac by a narrow orifice just admitting a fine probe, the orifice being situated on the anterior wall about 1 cm. above the lowest part of the sac. The duct below showed no obstruction and no dilatation. No dilatation of pancreatic duct.

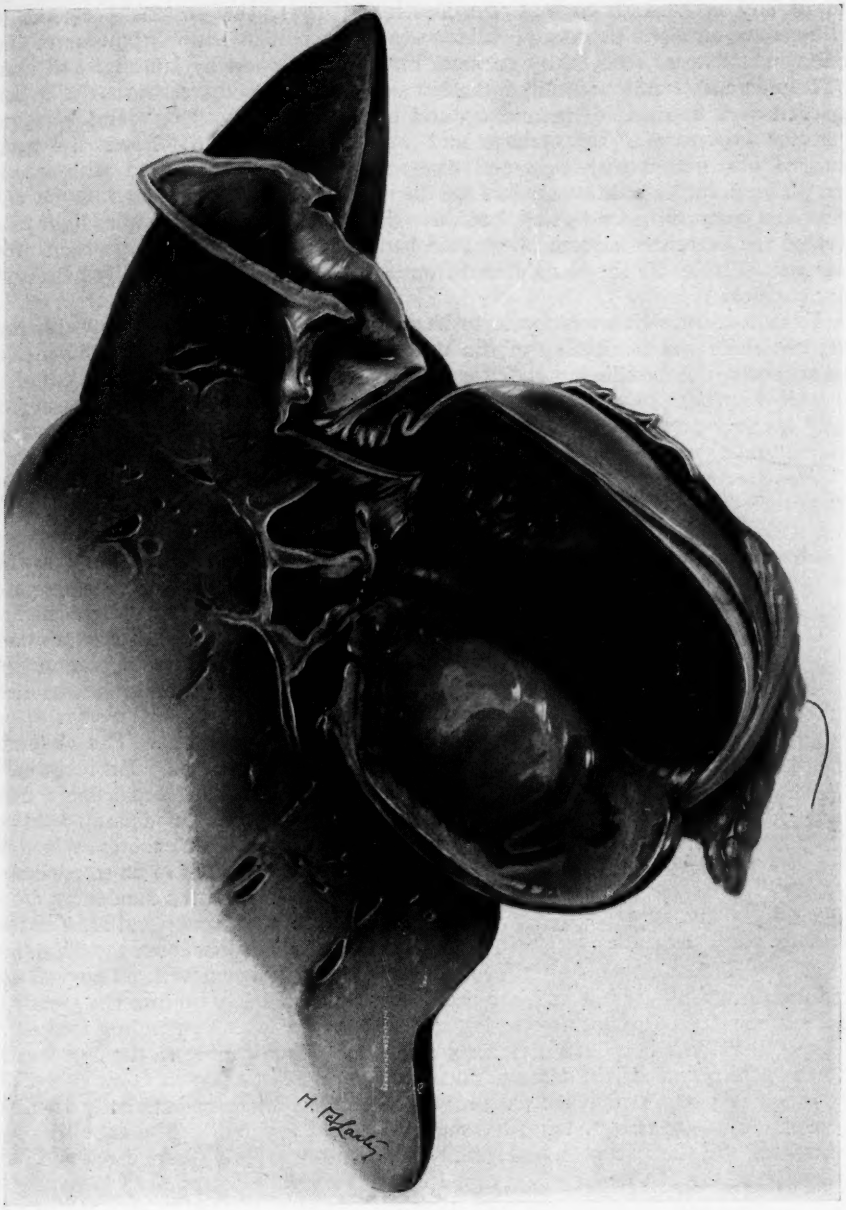

FIG. 212.—Post-mortem specimen from *Case* 1. (*From the London Hospital Museum.*)

Case 2.—M. S., a married women aged 34, was first seen on Nov. 1, 1932. She stated that for some years she had had indigestion, with occasionally rather severe pain. In 1925 she was operated upon in Manchester. The gall-bladder was said to have been diseased and was removed. It contained no stones. Six months later she had symptoms of intestinal obstruction which were relieved by enemata. In October, 1929, she was said to have acute pancreatitis, for which an operation was performed in Oxford, three tubes being inserted. Early in 1931 she went to a clinic and was fully investigated: the liver efficiency tests were all normal, the fasting blood-sugar did not rise after 50 g. of lævulose, the stools were normal and the diastatic index was within normal limits, the liver was not enlarged, and there was

no note of any abdominal tumour. In December, 1931, she became pregnant, and in August, 1932, when eight months pregnant, was again said to have symptoms of intestinal obstruction, which were relieved by enemata but were followed by jaundice and abdominal pain. The pain and jaundice steadily increased and she developed acetonuria. The condition was regarded as a hepatitis of pregnancy, and labour was induced on Sept. 8, 1932. She had a severe post-partem hæmorrhage and was much collapsed. Later she again had symptoms of obstruction with pain and distension which were relieved with eserine and morphia. The jaundice continued, and on Sept. 18 the liver was found to be enlarged. Since then the jaundice had persisted, but was said to vary. The stools were light in colour, but revealed the presence of some bile. Pain had been less, but had always been present in some degree. All her life she has suffered from asthma. There is no family history bearing upon her condition.

ON EXAMINATION.—She was found to be a fairly well-developed woman with profound jaundice, but there was no itching of the skin. There were large well-healed median and paramedian scars. A swelling was felt extending far down from the right costal margin which was thought to be the greatly enlarged right lobe of the liver. The blood showed a normal red and white count, but the hæmoglobin was only 82 per cent. There was no bile in the stools and no occult blood. She was seen by several physicians, who advised against operation as the condition was regarded as a hepatitis of pregnancy. I felt, however, that the severity of the pain and the complete absence of bile in the stools gave a faint hope that there might be an obstructive lesion. Her father and husband were both doctors, and they agreed that an operation gave her the one chance. The true condition was not considered.

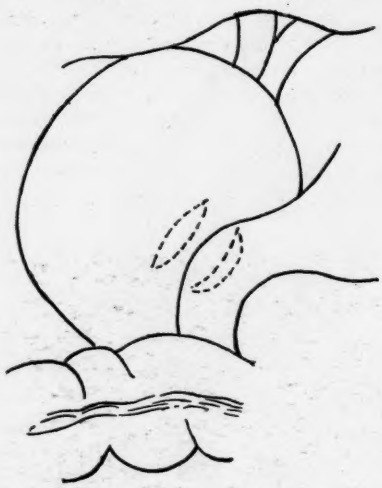

FIG. 213.—*Case* 2. Outline sketch of condition found at operation.

OPERATION (Nov. 15, 1932).—The abdomen was opened by an upper right paramedian incision. After many adhesions had been divided a large mass was felt behind the stomach and duodenum. On opening the gastrohepatic omentum the pancreas was seen to be normal, and the swelling found to be an enormous cyst lying behind and external to the duodenum (*Fig.* 213). A hypodermic needle was inserted and drew off thin bile. The cyst was then opened just above the duodenum and over a pint of thin bile removed. The wall was very thick and fibrous. A finger inserted into the opening passed freely up into the greatly dilated right and left hepatic ducts, but no opening could be felt below corresponding to the common duct. The gall-bladder had been previously removed. The opening in the cyst was anastomosed to an opening made in the adjacent duodenum, a tube passed down to the side of the cyst, and the wound closed. At first the patient was much collapsed and frequently vomited large quantities of bright green bile, but later she made good progress. The tube was removed on the third day and the wound healed well. The jaundice rapidly disappeared and has never returned. Since then she has lived a normal life and a year later appeared in perfect health, but the liver could just be felt. Six years after the operation she states that she occasionally has slight pain: one year before this was rather more severe, and she was tender over the liver. This was thought to be due to cholangitis, but it soon disappeared. Apart from this she is quite well except for her attacks of asthma.

Case 3.—I. D., a woman aged 25, was first seen on Jan. 18, 1938. She stated that at the age of 13 she had an attack of acute abdominal pain for which her appendix was removed in Leeds. It was said to be normal and its removal gave her no relief. She continued to have periodic attacks of pain, at first every few months and then every few weeks, but was quite well between. The pain was epigastric and very severe, causing her to double up. It had no relation to food. It caused her to vomit, and the vomit gave relief. She was often given morphia. At that time it never occurred at night. The attacks continued for five years, being unrelieved by diet or medical treatment. Seven years ago she had another

operation, the symptoms being thought to be due to a mobile cæcum, and this was fixed. She was better for a short while, but the attacks soon returned with the same severity and frequency as before. Two years ago she came to London and entered hospital. She was under investigation for one month, and being seen by her physician in an acute attack, was advised immediate operation. At the operation the gall-bladder was said to be adherent, but contained no stones. It was removed. For six months after this she was better and gained 2 st. in weight. At Christmas, 1936, while running upstairs, she had a sudden onset of her old pain. Since then the attacks have occurred with increasing frequency and now take place about once a week. The pain now usually occurs on rising in the morning and she is unable to take breakfast. It steadily increases until it causes her to roll about and sweat. She vomits at the height of the pain and this gives a little relief, but she nearly always has to have an injection of morphia. The attacks never occur at night. In between the attacks she is quite free from pain. She has never been jaundiced.

ON EXAMINATION.—She is a well-developed healthy looking girl. There are two well-healed abdominal scars, right upper and middle paramedian. There is marked tenderness under the upper rectus. A radiograph after a barium meal showed moderate duodenal ileus with some delay at the flexure. On Feb. 7 she was seen again in an acute attack, and during this there was a definite swelling under the upper right rectus which suggested the possibility of a diverticulum of the common duct or a dilated duodenum from obstruction.

OPERATION (Feb. 10, 1938).—Upper paramedian incision. Many adhesions: those between the colon, duodenum, and under surface of the liver were divided, the duodenum was pulled down, and a cystic swelling about the size of a tangerine orange revealed behind and above it. It was aspirated and thick bile withdrawn. The thick fibrous wall was then opened and the cavity explored with the finger, which could be easily passed into the greatly dilated hepatic ducts and the stump of the cystic duct. The opening of the lower end of the duct could not be felt. A lateral anastomosis was performed between the cyst and the duodenum, and the wound closed.

For eight days after operation she vomited profusely a bile-stained fluid, and was very ill and collapsed. She then improved rapidly and remained well for about eight months. Since then she has again had several attacks of pain, much less severe than formerly, and associated with some vomiting. It is probable that these are due to the duodenal ileus. She is otherwise well one year after operation.

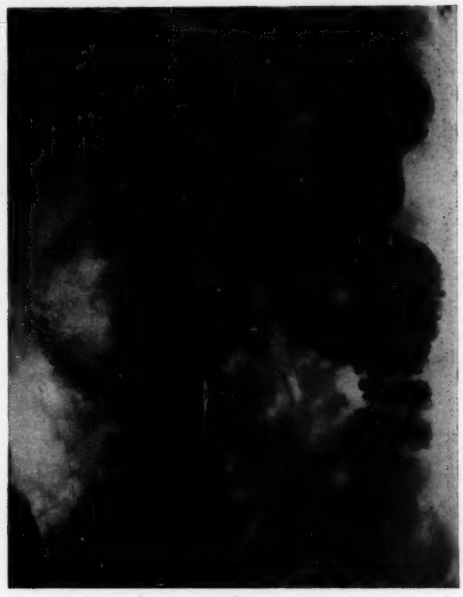

FIG. 214.—*Case* 4. Congenital diverticulum of the common bile-duct. Radiograph showing remarkable distortion of the duodenum.

Case 4.—A. W., a man aged 39, was seen at hospital on Jan. 10, 1939. Two weeks before he had been admitted for investigation on the medical side. He stated that twelve years ago he had begun to have attacks of biliousness and vomiting after taking fatty foods. Eight years ago he had an operation for hæmorrhoids, and ten days after this had had an attack of severe pain under the right costal margin, which passed up to the right shoulder. Seven years ago he had another attack, which was preceded by shivering, and during the attack he vomited. Since then the attacks had been increasing until they occurred every six weeks. Six years ago he was operated upon with a diagnosis of gall-stones, but he states that nothing abnormal was found and the abdomen was closed. He was better for a few months and then the attacks returned. Five years ago he became definitely jaundiced in one of the attacks, and this has recurred with all the subsequent attacks. During the last five months the attacks have been much more severe, and the pain and jaundice have been almost constant. During this time he has lost 1 st. in weight. There is nothing bearing upon the condition in his family history.

ON EXAMINATION.—He was slightly jaundiced. There was a well-healed right upper paramedian scar, much tenderness under the right upper rectus, and an ill-defined swelling above and to the right of the umbilicus. The liver and spleen were not palpable. Examination of the blood revealed a normal red and white count, with hæmoglobin 89. The fragility curve was normal. X-ray investigation after a barium meal revealed the duodenum stretched out in a wide circle, a cyst of the head of the pancreas being suggested (*Fig.* 214). There

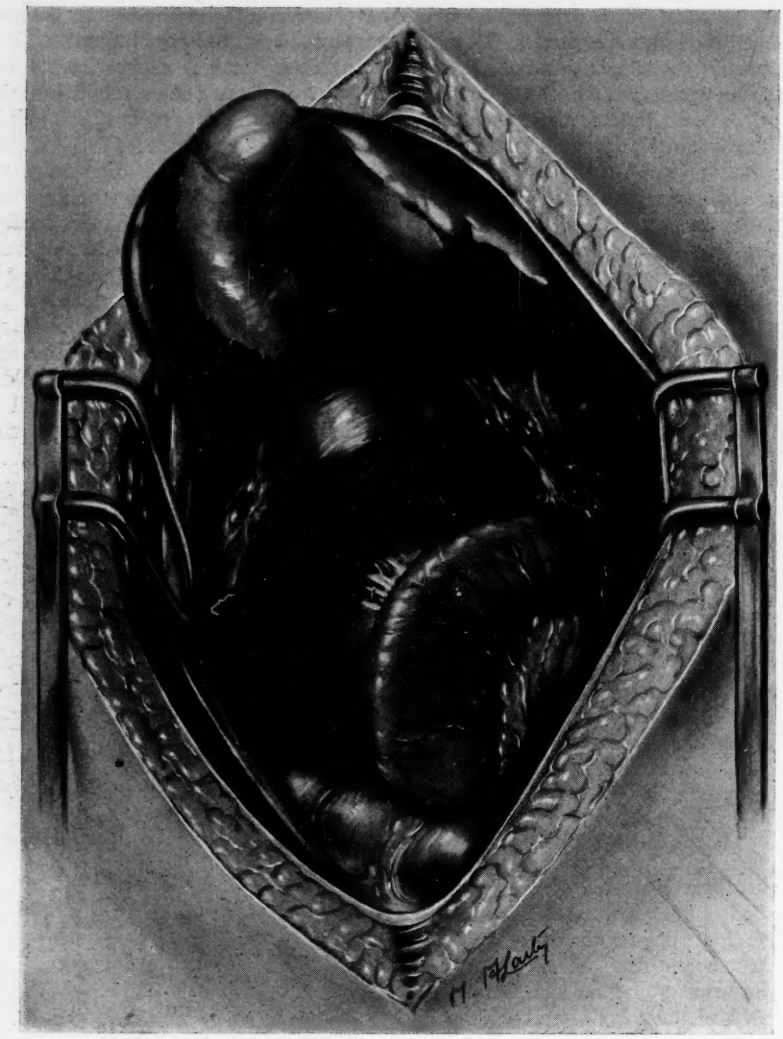

FIG. 215.—*Case* 4. Congenital diverticulum of the common bile-duct. (*From a sketch made after operation.*)

was no evidence of a stone in the common duct, and no sign of a gastric or duodenal ulcer. A positive diagnosis of congenital diverticulum of the common duct was made, and an operation advised.

OPERATION (Jan. 11, 1939).—Upper right paramedian incision. The gall-bladder was a little distended and œdematous, with somewhat thickened walls, but contained no stones. A large cystic swelling was felt above and behind the duodenum, and above and internal to it was seen and felt an enormously dilated common bile-duct (*Fig.* 215). The cyst was then aspirated and 16 oz. of bile-stained fluid removed. It was opened and explored. Above,

the common bile-duct opened into it by a single opening large enough to admit three fingers; below, a small valve-like opening could be felt on the inner side which would not admit the tip of one finger. The wall of the cyst was dense and fibrous, and greatly thickened. An anastomosis with an opening 1 in. long was made between the cyst and the overlying duodenum, and the wound closed. The patient made an uninterrupted recovery and has remained free of all symptoms to date.

Case 5.—K. J., a married woman aged 43, was first seen at hospital on Jan. 18, 1939. Three weeks before she had been admitted on the medical side. She stated that two weeks before admission she had first noticed a non-constant, non-radiating, and slight pain under the right costal margin. Subsequently the pain became worse and began to radiate round to the back and the right shoulder. The last four or five attacks had been so severe that she had rolled on the floor in agony. Each attack would last about an hour. At the age of 17 she had had her appendix removed for an acute attack, but since then had remained quite free from all abdominal symptoms until two weeks ago. She had never been jaundiced. She has two children and had normal pregnancies.

ON EXAMINATION.—She was a well-nourished, healthy looking woman with no trace of jaundice. The abdomen had lax walls with some tenderness on deep pressure below the right costal margin. No tumour could be felt. The blood showed a normal red and white count, with hæmoglobin 89 per cent. The radiographs showed that the gall-bladder failed to fill with dye. There were no shadows of gall-stones. There was, however, in all films, including those without the dye, an indefinite shadow external to the duodenum, which was possibly due to a thickened gall-bladder (*Fig.* 216).

FIG. 216.—*Case* 5. Congenital diverticulum of the common bile-duct. Radiograph showing the shadow of the diverticulum (the outline has been accentuated for purposes of reproduction).

OPERATION (Jan. 20, 1939).—Upper right paramedian incision. Uterus, tubes, and ovaries bound together by old adhesions. Some adhesions in region of old appendicectomy wound. No lesion in stomach. Firm adhesions between colon and gall-bladder. When these were freed the gall-bladder was seen to be normal in size and appearance, and contained no stones. A cystic swelling was then found above and external to the duodenum. It was aspirated and 14 oz. of thick foul-smelling bile-stained fluid removed. The cyst was opened and a finger could be easily passed up into the greatly dilated common duct above, there being only one opening. The cystic duct was not dilated. The lower opening into the common duct could not be found. The cyst wall was formed of dense, thick, fibrous tissue. A lateral anastomosis was made between the cyst and the duodenum, using the opening which had already been made into the cyst and which was about 1 in. long. Owing to the infection of the bile a tube was inserted into Morison's pouch and the wound closed.

The patient made an uninterrupted recovery, the tube being removed on the third day, and the stitches on the tenth day. She left hospital 16 days after operation and has remained well to date.

POST-MORTEM CASE

Case 6.—C. B., a girl baby aged 1 month, was admitted to the London Hospital on Sept. 9, 1911, under the care of the late Dr. Warner, with the statement that fourteen days before she had been constipated, this being followed by vomiting. Since then there had been increasing jaundice.

ON ADMISSION.—She was deeply jaundiced. The temperature was 99°. The eyes were sunken and the abdomen was distended. The umbilicus was normal, and the liver and spleen were not enlarged. A blood-count showed red blood-corpuscles 3,800,000, white blood-corpuscles 9300. There were 29 normoblasts and 2 megaloblasts while counting 200 white corpuscles. On Sept. 14 the jaundice was more intense, and the gums were spongy and bleeding. There was a hæmorrhagic and purulent discharge from the vagina, but no joint symptoms. On three occasions since admission the temperature had risen to 100·5°. On Sept. 15 she collapsed and died.

AT AUTOPSY.—I am indebted to the notes of Professor Turnbull for the following account of the condition of the biliary apparatus (P.M. No. 955, 1911). There was a sac uniting the neck of the gall-bladder, the hepatic ducts, and the retroduodenal portion of the common bile-duct. It was a large flaccid sac between the gall-bladder and the duodenum. No dilatation of the gall-bladder. Communications patent to probe between the sac and the gall-bladder, hepatic ducts, and through caruncula major of Santorini with the duodenum. Small aperture in right margin of sac, surrounded by torn peritoneal adhesions. Bile and blood in peritoneum. Very slight dilatation of bile-ducts.

In looking through these cases certain facts of great practical interest arise, which will be considered more fully in the detailed discussion, but may be summarized here. The first is that although the pathological changes are so remarkably constant, and indeed seem to differ only in degree, the symptoms are astonishingly protean in nature. In the first case, the three symptoms which are always regarded as characteristic, namely, pain, jaundice, and tumour, were absent, and the clinical picture was altogether identical with that of advanced Banti's disease with ascites. In the second case the similarity to a hepatitis of pregnancy was almost complete, although the past history might have caused a little doubt. The pain and the presence of a swelling during the attacks in the third case were very suggestive, and sufficient to give rise to a suspicion of the true nature of the disease, but at no time had she ever been jaundiced. The fourth patient alone showed the typical symptoms of pain, jaundice, and tumour, although the latter was ill defined and much less evident than would have been expected from the fact that the cyst contained 16 oz. The symptoms, however, with the X-ray appearance, were sufficient to allow of a positive diagnosis being made. In the fifth case, the symptoms, appearing in a woman of 43, with only a two weeks' history and no previous trouble, were characteristic of gall-stones, and she had never had jaundice; nor was there pyrexia or a history of rigors, although the bile was grossly infected. No tumour could be felt in spite of the fact that the cyst contained 14 oz. The only factor which might have led to a suspicion of the true nature of the lesion was the appearance on X-ray examination. The sixth case apparently had had jaundice associated with symptoms of scurvy, passing on to acute peritonitis from rupture of the diverticulum.

The second remarkable fact is that in 3 of the 5 cases operations had been undertaken, all by skilled and experienced surgeons, for symptoms very suggestive of gall-stones, and yet the pathological change had been missed. In the second case there had been 2 such operations; in the third case, 3; and in the fourth case, 1. Nothing could give greater force to the argument that in every operation for gall-stones the common duct must be examined, and this more certainly so if no stones are found in the gall-bladder. The reason that the diverticulum was overlooked was probably due to the fact that it lay in greater part behind the duodenum and colon, and was covered by membranous sheets passing up to the edge of the gastrohepatic omentum and to the gall-bladder.

The third point of importance is that in spite of the fact that the literature lays stress upon the very high mortality of operation, yet 4 of the 5 cases made an uninterrupted recovery, and it is possible that in the first case, although the post-mortem revealed widespread thrombosis, this might have been secondary to the splenectomy; and if this condition had been recognized at first, the spleen not removed, and a choledochoduodenostomy carried out, the patient might have recovered and the condition of the liver and spleen have returned to normal—a forcible reminder of the fact that after an abdomen is opened the viscus in which disease is expected should be examined only after the rest of the abdomen has been explored, lest the attention become so fixed that the general exploration is forgotten.

PATHOLOGY

The pathological changes in all the reported cases, as well as in my own, are remarkably alike, and consist of the presence of a cystic dilatation of that portion of the common bile-duct lying above the duodenum. The cyst, although more or less spherical, is always eccentric and differs entirely from the uniform dilatation of the duct seen above an obstruction. The swelling nearly always extends to the right, as in all my cases and those of Fowler, Waller, Morley, Wright, McWhorter, and Judd (*Figs.* 213–222), but in those reported by Heid and Budde it was said to extend to the left. When the cyst is opened the orifices of the common duct and the hepatic duct are seen to be in line on the inner surface, and often indeed lie at the ends of a shallow groove (*Figs.* 212, 223). The cyst is, in fact, more like a saccular than a fusiform aneurysm. Hence the term "congenital diverticulum", as suggested by Wright, is more correct than "congenital cystic dilatation".

The diverticulum lies behind and above the duodenum, and, as it enlarges, spreads upwards to the liver, outwards towards the right renal fossa, and downwards to the pelvis. The duodenum is usually pushed downwards and inwards, but may be stretched and flattened over the surface. Zinninger states that the enlarged cyst may come to be in front of the duodenum. The hepatic flexure is pushed downwards and outwards. At operation the diverticulum may vary in size from that of a tangerine to a swelling which passes right down to the pelvis, and is mistaken for an ovarian cyst or an advanced pregnancy. It is, as a rule, clearly visible, but if only of moderate size may be hidden by membranous adhesions passing from the duodenum to the liver.

Below, the pathological change seems to be sharply limited to that portion of the duct above the duodenum, but above its termination is less constant. Generally there are two openings above, that of the common hepatic, and that of the cystic duct; that is to say, the common hepatic duct does not participate in the diverticulum. In my fourth and fifth cases, as in those reported by McWhorter, Saint, Morley, Wright, and Waller, this was the condition. In other cases, there are three openings, the common hepatic duct being involved and the two hepatic ducts opening separately into the cavity. This was seen in my first three cases and in the sixth case, and in that of Fowler.

The contents of the sac are usually thin bile-stained fluid, the quantity of which varies greatly from a few ounces to several pints; Zinninger says from 30 to 8000 c.c. Saint states that it may be several litres. In Reel and Burrell's case it was said to

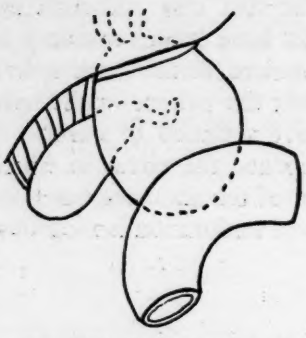

FIG. 217.—Outline tracing of illustration of Fowler's case.

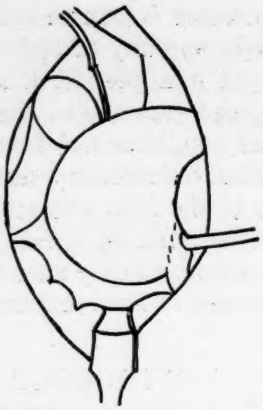

FIG. 218.—Outline tracing of illustration of Waller's case.

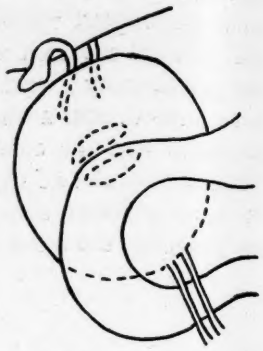

FIG. 219.—Outline tracing of illustration of Morley's case.

FIG. 220.—Outline tracing of illustration of Wright's case.

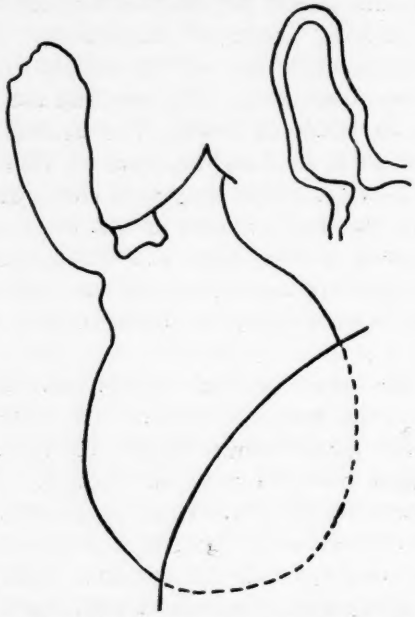

FIG. 221.—Outline tracing of illustration of McWhorter's case. *Inset*, Gall-bladder showing hypertrophy of sphincter muscle at neck.

FIG. 222.—Outline tracing of illustration of Judd and Greene's case.

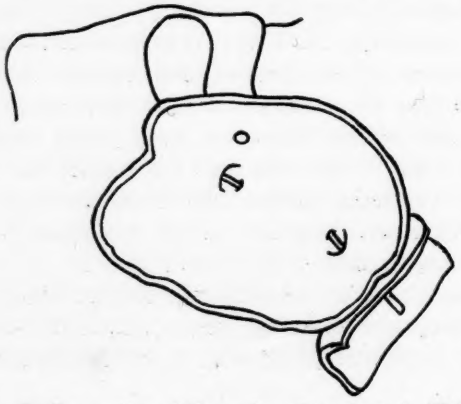

FIG. 223.—Outline tracing of illustration of specimen in Wright's case.

amount to 8 litres. In Wyllie's case the bile was dark green and viscid in character, whereas in Russell's case white bile was present. These changes probably depend upon the amount of obstruction; if nearly complete, the bile is likely to be white, owing to failure of the liver function, as in some cases of carcinoma of the head of the pancreas; if, however, the obstruction is incomplete, and there is free communication with the gall-bladder, the concentrating function of this viscus may cause the bile to become thick and viscid. In some cases the bile is infected. In my fifth case it was thick and foul, and resembled the contents of the small intestine. In Saint's case it was infected with the typhoid, and in Zinninger's case with the paratyphoid, bacillus. McWhorter states that the contents are sometimes purulent bile-coloured fluid, but in his 48 collected cases, only 14 were infected. In none of my cases were there any structures in the diverticulum or ducts resembling gall-stones, and this is the usual finding. In McWhorter's case there were a few black stones in the diverticulum, and the hepatic ducts were filled with small stones. He states that stones were present in the cases of Dreesman, Wagner, Arnolds, and Budde, but in all these cases they were minute fragments or incrustations.

In my five operative cases the wall was dense, thick, fibrous, and tough, the cut edge appearing yellow, and the wall only collapsing in part when the cavity was emptied. In the first case it was described post mortem as being $\frac{1}{3}$ cm. in thickness. In the post-mortem case where rupture had occurred the wall was thinner and flaccid. In the majority of the reported cases it was also noted as being thick and fibrous, but in a few it has been described as thin and very friable, so that it ruptured on manipulation, as in Reel and Burrell's and Waller's cases. Fowler also states that in his case the wall was very thin. In Zinninger's case, which was infected, the walls were œdematous. The peritoneum is usually densely adherent over the diverticulum, and can only be separated with difficulty. The lining membrane may be epithelial; in Zinninger's case the mucosa was said to resemble that of the gall-bladder; and Wright states that his specimen was lined by epithelium. In others it is much ulcerated, as in my first case, and Morley says the mucosa is usually absent. On section the wall shows dense fibrous tissue often with muscle-fibres. In Budde's case there were a few gland tubules present. In Reel and Burrell's case there were small tubules lined with a single layer of columnar cells like small bile-ducts, and occasional areas of liver substance. Similar tubules lined by columnar epithelium were also described by Rostowzew. McWhorter states that in 20 of 23 cases examined microscopically there was entire absence of an epithelial lining.

The ducts above, whether common hepatic or separate, are, as a rule, greatly dilated, as may be seen from the various diagrams of published figures; but this dilatation is cylindrical and is in no way a part of the saccular diverticulum. In all 5 of my cases a finger could easily be inserted, and in the third case, where there was only one opening, three fingers were easily passed. In the first case the post-mortem showed that the walls of the dilated ducts were much hypertrophied. This, however, is not constant. In my sixth, or post-mortem case, it is stated that there was very little dilatation of the bile-ducts; a similar absence of dilatation was noted in the cases of Willis, Saint, Wright, and Morley. In Wright's case the opening of the common hepatic duct was guarded by a valvular fold. On the other hand, the cases of Zinninger, Wyllie, McWhorter, and Fowler showed great

dilatation of the ducts. In the cases collected by McWhorter the ducts were dilated in 30 and normal in 2. The dilatation does not appear to pass up to the intrahepatic ducts. In my first case (that died) and in the sixth case, there was no evidence of dilatation of these ducts. In the few cases in the literature where this point is mentioned there seems to have been no dilatation.

It is remarkable that in the greater number of cases the gall-bladder is of the normal size, even if the lower part of the cystic duct be dilated. In none of my cases was there a dilatation such as is so constantly seen with examples of carcinoma of the head of the pancreas or chronic pancreatitis; although in my fourth case it was a little distended and œdematous. In Russell's case, however, it was described as being extremely dilated, and in the series collected by McWhorter dilatation was present in 17 and absent in 16 cases. In the 5 cases reported by Russell, Seeliger, Dreesman, Mayesima, and Arnolds, the viscus was sufficiently enlarged to form a second tumour, which could be felt in life above the main mass of the diverticulum. In McWhorter's case the muscle of the gall-bladder formed a sphincter-like thickening at the neck (*Fig.* 221).

The greatest interest centres around the condition of the common duct below the diverticulum. In all my cases the opening was apparently narrowed, and in only one could it be felt by the examining finger. In this case, and in the one that came to post-mortem, the opening was high up on the inner side of the cyst. This is the condition which has been noted in most of the reported cases, the opening being greatly constricted; but even when it could not be found it was usually stated that bile was being passed into the intestine, so that the obstruction was not complete. In 3 of my own clinical cases, indeed, there was no jaundice, and it was also absent in the cases reported by Smit, Veau, Saint, Zinninger, Dickson Wright, and Waller. In Lavenson's case the terminal duct was said to be completely obstructed. In only one case—that of Fowler—can I find the statement that the lower duct was greatly dilated. As a rule, the narrowing does not extend down to the ampulla, and the pancreatic duct is unaffected. Many authors lay stress upon the fact that the opening is high up on the inner side and is guarded by a valve-like fold of mucosa. In fact, as is seen in the diagrams of Wright's case and my own (*Figs.* 212, 223), the hepatic duct above and the common duct below appear to open at the ends of a shallow groove. This, of course, is the appearance that would be expected with a saccular diverticulum. On many occasions the analogy of this high opening on the inner side with the position of the ureter in congenital hydronephrosis has been pointed out.

As the diverticulum enlarges it may cause pressure. The duodenum is not uncommonly flattened over it and somewhat dilated. The dilatation may, however, as in Morley's case, and in a lesser degree in my third case, be due to duodenal ileus, which Morley considers arises from pressure of the diverticulum on the root of the mesentery.

In marked contradistinction to congenital obstruction of the common bile-duct and carcinoma of the ampulla or head of the pancreas, the obstruction from the diverticulum seems to affect the liver but little. In none of my cases was there evidence of true cirrhosis. In Wyllie's case there was a mild cirrhosis, and in McWhorter's 48 collected cases there was cirrhosis in 14 and hepatitis in 3 cases.

In some of the advanced cases there is ascites and enlargement of the spleen. The ascites may be dependent upon cirrhosis of the liver, or, as would appear to

have been the cause in my first case, to pressure upon the portal vein. In this case there was no true cirrhosis, but the portal, splenic, and superior mesenteric veins were thrombosed.

AETIOLOGY

It will be noted at once that 5 out of my 6 cases are females, and this sex ratio has been constant in all the collected lists, it being usually given as 80 per cent females. The reason for this sex distribution is quite unknown. It certainly has no relationship to the greater frequency of gall-stones in women, for stones are very rare in the diverticulum and even cholecystitis has not been frequent.

Most of the patients have been relatively young and have often had a prolonged history. In my sixth case, found in the post-mortem records, the girl was only 10 months old. The first patient was 16; the second 34, but with a history dating back to the twenties; the third was 25, but her symptoms commenced at 13; the man was 39, but also had a history of 12 years. The last case, it is true, was remarkable in that she was 43 and had only a two weeks' history, but from the size and thickness of the wall of the cyst it was manifest that it had been present for a long time. Willis states that 50 per cent of the reported cases are under 15. In Wright's and Judd's cases, aged 15 and 13 respectively, symptoms went back to early infancy, and in the case operated upon by Pratt and reported by Morley, the patient was only 6½. The youngest case was that of Oxley, who was only 5 weeks old. On the other hand, the oldest patient was the one reported by Reel and Burrell, who was 56, but she had had a tumour for twenty years.

No true hereditary history has ever been found. The nearest was in Morley's first case, where there were 2 brothers and 1 sister, all born before the patient, and who all died with jaundice in infancy, but there had been no post-mortem examinations and the cause of the jaundice was therefore unknown.

The cause of the diverticulum has led to much discussion: the fact that the opening from the diverticulum to the common bile-duct below, and often, indeed, a portion of the common bile-duct itself, is narrowed, gave rise to the belief that the primary lesion is an obstruction of the duct which has been followed by the dilatation above. Hill and Ramsey were of this opinion, and believed that the obstruction was partial and intermittent and so led to an increasing dilatation. In this connexion Rostowzew made the interesting observation that in his case the lower part of the duct ran an abnormal course through the duodenum, passing from left to right, thus causing a kink. Budde also described the ampulla in his case as lying on the right and anterior part of the duodenum, although he did not believe that this was the primary cause. Wettwer was of the opinion that the lower duct passed through the wall of the duodenum from below up; while Heid, Seeliger, and Edgeworth all believed that there was a congenital narrowing of the duodenal portion of the duct.

It is, however, almost certain that the primary cause is not a congenital or acquired obstruction, for the dilatation is entirely unlike that caused by all the known obstructions, such as impaction of a stone in the ampulla, carcinoma of the ampulla or head of the pancreas, and chronic pancreatitis; the dilatation in these cases being uniform or fusiform. As Waller also pertinently points out, a congenital obstruction would cause symptoms soon after birth, whereas in many cases the choledochus has performed its functions for some years. The presence

of a valvular fold at the opening of the common duct below has been noted by many observers, and Rostowzew, Heid, Wettwer, and Smit have described similar folds at the openings of the upper ducts. The presence of this fold over the lower opening and the situation of the opening high up on the inner side give, as has been noted by many, an analogy with congenital hydronephrosis. It is manifest, however, that these valves could not have been the primary cause, for they occur at the junction with the diverticulum, and if there were no diverticulum there could be no valves. When the diverticulum is present, however, they could cause an obstruction by flattening and thus lead to an increase in the size of the sac; possibly in some cases they could prevent the distension involving the upper ducts and gall-bladder. The obstruction so caused might be intermittent, and it is of interest to note that in several patients, as in my third case, the tumour varied in size, increasing during an attack of pain, or, as in Wright's case, after the ingestion of food. Judd and Greene give a diagrammatic representation of the method by which the valvular opening is stretched as the cyst fills and the cavity thus empties intermittently (*Fig.* 224).

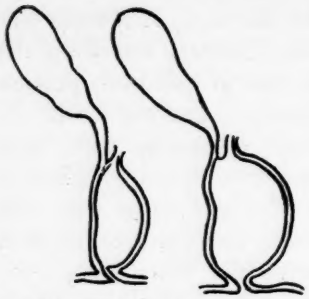

FIG. 224.—Showing how increased distension may overcome a valvular obstruction (Judd and Greene's case).

It has also been noted in some cases that the symptoms have a relationship to pregnancy. In my second case the jaundice arose in the later months of pregnancy, so that the condition was mistaken for a hepatitis. In McWhorter's case the symptoms were always more severe after the fourth month of each pregnancy, and the pain was much worse after the birth of the seventh child. Goldammer thought that the compression of pregnancy might increase the obstruction, while McWhorter thinks that the fall of pressure after delivery might cause kinking, and states that in two of the reported cases the symptoms followed pregnancy. It would seem, however, that the exacerbation of the symptoms might equally well be due to the increased work thrown by the pregnancy upon the already distressed liver. My fifth patient had had two normal pregnancies before her symptoms commenced.

Although obstruction may, therefore, be a secondary factor and may increase the size of the swelling, it would seem probable that the diverticulum itself is primarily due to a congenital anomaly. Dreesman, in 1906, put forward the view that the pouch was caused by a congenital weakness with subsequent dilatation, a view which has later been supported by Lavenson, Ebner, Weiss, and Goldammer; while Ebner and Lavenson specified that the weakness was in the muscular tissue, Waller believed that there is also a deficiency in the elastic tissue. The similarity in the appearance of the lesion in all reported cases, the constancy of its site, the saccular character, and the frequency of a thick wall to the diverticulum all strongly support the view that the lesion is a congenital fault. The interesting finding of Heiliger, which has been quoted in many of the monographs, of a small diverticulum, $3 \times 2\frac{1}{2}$ cm., in an almost mature fœtus, strongly supports this view. He believes that the diverticulum may arise in a small bud of an accessory duct. Budde, owing to the abnormal position of the ampulla of Vater in his case and the presence of a few gland tubules in the wall, suggests that there is an abnormality in the rotation of the mid-gut, and a primary diverticulum which is the result of an accessory

pancreatic rest; but unless these tubules, and the few, less definite, seen in the cases of Reel and Burrell, and of Rostowzew, be regarded as pancreatic, there is, as Morley says, no real evidence that pancreatic tissue has ever been discovered.

It is probable, therefore, that the diverticulum is dependent upon the presence of a small congenital weakness in the lateral wall of the duct, which may arise at the site of an accessory duct, and that at first it is dormant; but as it increases in size, like a saccular aneurysm, the lower part of the duct becomes obstructed, which in turn leads to greater pressure upon the diverticulum until in time symptoms are produced.

SYMPTOMATOLOGY

Perusal of the literature would lead one to infer that the symptoms are fairly well defined, and this in spite of the fact that so few cases were correctly diagnosed. Saint and Zinninger, both writing in 1932, state that the condition was diagnosed correctly before operation in three cases only: by Neugebauer in 1924, by Iselin in 1927, and by Taylor in 1928. My own six cases show what entirely different pictures may be presented. Most frequently the dominant symptoms have been severe pain and jaundice resembling gall-stones. Here, again, the reported cases show that the majority of the patients have been under the age of 15, and it might be thought that since gall-stones are rare at this age the true condition should be suspected, but of my 6 cases 3 were over 30 and 1 was 25. In 2 of them the true diagnosis was considered before operation because of the long history, but in the woman of 43 the symptoms had commenced only two weeks previously.

Wright states that the symptoms appear in three groups: (1) Those with a large tumour; (2) Those with pain and jaundice; (3) Those with an acute abdominal condition with pain, tenderness, vomiting, and rigidity. To a certain extent this is true. The patient reported by Dickson Wright complained chiefly of a large tumour which had been regarded as a pregnancy. In my first case, the dominant symptom was enlargement of the abdomen, and in Morley's case the condition had resembled an ovarian cyst, but she had had pain and jaundice. The group with pain and jaundice is the largest, but in many there was also a tumour, and not uncommonly there may be no jaundice, as in three of my cases. The variety with acute abdominal symptoms is of special interest. In *Case* 6, discovered in the post-mortem records, there were acute symptoms due to rupture of the diverticulum. In Zinninger's and Saint's cases there was no perforation, but the bile was infected with typhoid and paratyphoid bacilli. In my own *Case* 5 the bile was infected, but there were no acute symptoms. It is in these cases that the rigidity and tenderness are so marked that a diagnosis of perforated peptic ulcer or of acute cholecystitis is made.

These groups are, therefore, not sharply defined, and it is perhaps the combination of the different symptoms which should help in making a diagnosis. As Wright says, "The clinical picture should in all cases be clear enough to enable a diagnosis to be made", but it very rarely is, probably because the lesion is so rare that its possibility is not considered.

In my own cases, the most frequent and most definite symptom has been pain, which was severe in four cases. In all of these it was typical of biliary colic and required the administration of morphia for its relief. In three of them, indeed, an operation had been carried out for gall-stones, and in two the gall-bladder had

been removed. It seems inconceivable that under these conditions the lesion could be overlooked. I have in previous communications laid stress upon the fact that gall-stones may be present in the common duct when the gall-bladder appears to be healthy, and these cases further emphasize the necessity of examining the common duct in all cases of operation for gall-stones, and more especially so if the gall-bladder appears to be normal. In some patients the pain is much less severe, and in the first of my series it was entirely absent. In many of the reported cases it has been only a slight dyspepsia, usually described as a bilious attack. When severe it is in its early stages at least always periodic, and thus more closely resembles biliary colic. In the commencing years attacks may occur annually, but they gradually become more frequent until severe attacks are seen as often as two or three times a week, and the patient's life becomes unbearable. The pain commences in the right hypochondrium under the right costal margin, radiates to the back and up to the right shoulder so that in its distribution it is indistinguishable from biliary colic. In fact, it is biliary colic, but not due to a stone.

Jaundice has been regarded by several writers as the most constant of the symptoms, and when Waller wrote his paper in 1917, he stated that it was only absent in one case, that of Smit. In 3 of my 5 clinical cases, however, there had never been a trace of jaundice. In the cases published by Zinninger, Willis, Saint, Dickson Wright, and Bolle, since Waller's communication, there had never been icterus. When present it may be extremely variable. Thus in Waller's own case the patient had never noticed any jaundice, but the urine was dark green and contained bile-pigment; in others, there has been only slight yellowness in the attacks, but it may progress until in the last attack it is complete and constant as in my own second case. It is in such a stage that the disease is likely to be mistaken for chronic pancreatitis, hepatitis, or carcinoma. Although the jaundice may then appear to be complete, with a urine heavily laden with bile and pale stools, the occasional presence of bile in the stools may give a clue to the diagnosis.

The presence of the diverticulum may give rise to a palpable tumour, but its size is extremely variable. In *Case* 5 no swelling could be felt either by members of the medical staff or by myself. In *Case* 4 it was indefinite, and was probably felt only because the past history had suggested the diagnosis. In *Case* 3 it was manifest only during the attack of pain, and although carefully sought for could not be felt in the intervals. In *Case* 1 it was entirely hidden by the ascites. No tumour could be felt in the cases reported by Fenger and McWhorter. On the other hand, the swelling may, as already described, be so large as to be mistaken for a pregnancy or ovarian cyst. It is usually stated to be about as large as a fœtal head. The tumour is more or less spherical, smooth in outline, and elastic, or, if sufficiently large, definitely fluctuating. It usually shows some degree of mobility, especially in the lateral direction, and may move slightly on respiration. Being situated mainly on the right side, it extends from the liver above, with which its dullness is often continuous, for a varying degree down to the pelvis, but it does not generally pass back to the loin. Its size may increase and it may become more tense, either during the attacks of pain, as in my third case and the cases of Taylor, Wyllie, and Fowler, or after the ingestion of food, as noted by Judd, Wright, and McWhorter.

Generally the liver is not palpable or is only slightly enlarged, and as a rule the gall-bladder cannot be felt, but, as already mentioned, in five reported cases

it was sufficiently distended to form a second palpable tumour above the larger mass.

The X-ray examination may be helpful or confusing. There are, as a rule, no shadows on the direct X-ray films, but in some cases, as in *Case* 5, there may be an indefinite shadow of the diverticulum above and to the right of the duodenum. After the dye such a shadow may become more definite, but the gall-bladder shadow is not usually evident, and thus the diagnosis of cholecystitis may appear to be confirmed. In Dickson Wright's case, however, the gall-bladder shadow was well defined and was comma-shaped from flattening over the top of the cyst, and the cyst wall itself showed small areas of calcification. There was also a lyre-shaped area of calcification in the position of the hepatic ducts. In *Case* 3 the dilated hepatic ducts were clearly visible in the radiograph taken about one year after operation. In Reel and Burrell's case there was a large shadow extending upwards and pushing the liver and diaphragm up to the 8th space. Sometimes, as in *Case* 4, the distortion of the duodenum may suggest the presence of a cyst behind it.

In many cases vomiting has been noticed in the attacks. As a general rule this appears to be due to the severity of the pain, but it is of interest that sometimes the vomit contains bile, and it would appear as though this symptom occurred after the attack was over with the passage of large quantities of bile into the duodenum. In Morley's case the vomiting was regarded as due to duodenal ileus depending upon pressure on the root of the mesentery; and in my own third case, in which vomiting was excessive, especially after the operation, some degree of duodenal ileus was present, this case therefore appearing to support Morley's view. Where there has been an acute onset, either from infection of the diverticulum or from rupture, vomiting of the peritonitic type may be present, and pyrexia or even rigors may be seen. There will also probably be other evidence of peritoneal infection, such as tenderness, rigidity, and abdominal immobility.

In long-continued attacks of pain there is often a considerable degree of wasting, but many of the patients are well-developed and appear to be healthy between the attacks. In the same way anæmia is found only in those who are severely ill. In *Case* 1 pressure of the cyst had led to thrombosis of the portal vein, with ascites and enlargement of the spleen. A splenomegaly has been reported in other cases, as has ascites, but it is possible that these two changes may be dependent upon a secondary cirrhosis of liver and not upon thrombosis of the portal vein. In advanced cases the urine may be loaded with albumin, and œdema of the legs may occur.

If the patient be left without surgical treatment the progress appears to be inevitably downwards. Rupture or infection may lead to a rapid termination, otherwise the progress is slow. Gradually the back pressure causes a failure of liver secretion, or pressure upon the surrounding viscera interferes with their function. Even without these changes the patient may become exhausted and worn out from the severity of the pain, the frequency of the vomiting, and the prolonged jaundice. Zinninger found that in many of his collected cases the condition had not been recognized at operation, and in practically all of these the patient died. McWhorter also states that all cases not operated upon died.

With so wide a variation in the clinical picture it is not surprising that difficulties in diagnosis have often arisen. The larger tumours have frequently been mistaken for echinococcic, pancreatic, mesenteric, retroperitoneal, hepatic, or

ovarian cysts, for hydronephrosis, or hydrops of the gall-bladder. In my own series, the most frequent error had been a diagnosis of gall-stones, and operations had been performed in this belief. If the jaundice is persistent a carcinoma of the head of the pancreas or of the common bile-duct will be simulated, while if there are inflammatory changes the picture will more closely resemble an acute cholecystitis or even a perforation of a peptic ulcer.

TREATMENT

Since the evidence is so definite that the condition is progressive and that all cases left unoperated upon appear to die ultimately of the lesion, operative treatment should be undertaken. In the earlier published lists the operative mortality was extremely high. As Morley points out, this was due to two factors: firstly, the condition was not diagnosed and the operation was deferred until the patient was extremely ill from prolonged pain, jaundice, and pressure; secondly, the surgeon was often unconversant with the condition. In many of the cases, indeed, the lesion has been entirely overlooked, and either the abdomen closed or some useless operation, such as a cholecystectomy, performed. This ought never to happen, and could not occur if the common duct were examined. In others the diverticulum was discovered, but the surgeon, not realizing the pathology, carried out some procedure which was either too extensive or was unlikely to be successful.

The majority of the earlier cases were treated by external drainage, a method which is likely to fail owing to the constant and complete loss of bile and the risk of infection of the ducts. Waller, in 1917, found that there had been reported 21 cases of external drainage, all of whom died, and even in 1928 Judd found that this method of treatment had been fatal in nearly every case. In some a second operation was performed to anastomose the sinus or the opening in the cyst with the duodenum. Morley reported in 1923 that of 8 such cases on record, there were 5 recoveries. Sometimes the surgeon, finding a cyst, attempted to dissect it out. This is always a very hazardous procedure as the peritoneum and surrounding tissues are densely adherent, and if the cyst were large would entail a most prolonged and exhausting operation. Wright in 1924 said that there had been 3 extirpations which naturally were fatal. But McWhorter's case, published in the same year, showed a cyst containing 1 pint. He dissected it out and anastomosed the dilated hepatic duct with the duodenum, excised the cyst and gall-bladder, and the patient made a complete recovery. Anatomically this would appear to be the best procedure, as the large diverticulum, in which the bile might stagnate, would be completely removed and a normal passage re-established. It is generally, however, much too prolonged and severe a measure to undertake with such gravely ill patients.

So poor had been these early results that even in 1935 Dickson Wright stated that "the operative results are very poor and choledochoduodenostomy always results in cholangitis with eventually fatal results", and later "the operative mortality is 80 to 90 per cent and the results of operation are deplorable". More recent experience shows, however, that these conclusions are unjustifiable. Since the cyst is found at operation to be firmly bound to the duodenum, which is often stretched over it, it becomes an extremely easy measure to make adjacent openings and anastomose the two, thus giving free passage for the contents of the diverticulum to the duodenum. The first anastomosis was carried out by Swain in

1894, who carried out a choledochojejunostomy using a Murphy's button, the patient recovering. The first successful choledochoduodenostomy was that of Bakeš in 1906. All the more modern writers state that this is the operation of choice, a view with which I am in entire accord. When Waller wrote his magnificent monograph, his and Bakeš' case were two of the five recoveries reported by all methods. In Wright's series there had been 4 such operations with 2 recoveries. It is true that Bull, writing only this year, reports a case where choledochoduodenostomy was performed some three weeks after a preliminary drainage, and the cyst refilled, requiring two subsequent operations for drainage before a cure resulted. This, however, must be a very unusual result, and suggests that for some reason the anastomosis was not acting efficiently.

In my own series of 5 operative cases the position of the anatomical structures was such that when once the nature of the lesion was determined a primary anastomosis seemed the only natural treatment and was performed in them all. The first case, with thrombosis of the portal, splenic, and superior mesenteric veins, died; but the other four made complete recoveries. One was performed seven years ago, and the patient's life was undoubtedly saved by the procedure. She has not yet developed cholangitis, and although it is possible, as Dickson Wright claims, that all the cases may develop this complication and die from it, such a dismal view should not be accepted without evidence. I know of no such case which has been reported in the literature. Even should it prove true, many of these dangerously ill or chronic invalids may be given many years of health and happiness.

SUMMARY

A series of 6 new cases of the rare condition of diverticulum of the common bile-duct is reported. Five of these were diagnosed at or before operation, and of these 4 operative recoveries are recorded. The other case was discovered in a search of the post-mortem records and had not been recognized before death. The pathological changes are reviewed, the aetiology considered, and evidence produced to show that the lesion is probably a primary congenital diverticulum. The protean nature of the symptoms is discussed and the danger of overlooking the condition at operation is stressed. It is suggested that a primary lateral choledochoduodenostomy is the operation of choice, and that it should always be performed before the health of the patient is seriously deteriorated. Under such circumstances these cases show 80 per cent of recoveries.

I am greatly indebted to Prof. Turnbull and Dr. Woods for their help in looking up the post-mortem records; to Mr. Clark of the Registrar's department for his investigation of the clinical records; and to Miss McClarty for her two beautiful illustrations.

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CHRONIC ULCERATION OF THE GREATER CURVATURE OF THE STOMACH, WITH A CASE REPORT

By R. SHACKMAN and F. H. KEMP

THE predilection of certain pathological processes for particular sites is not only of academic interest but may be of diagnostic importance. The occurrence of ulceration on the greater curvature of the stomach is so rare, a fact in direct contrast to the relative frequency of the condition on the lesser curvature, that it merits great consideration before the diagnosis is accepted as being other than malignant.

R. Maingot (1935), G. B. Eustermann and D. C. Balfour (1936), and J. Morley (1937) have emphasized the difficulties met with in early diagnosis of gastric ulceration and the relative significance of the site in the differential diagnosis; and all the available data emphasize the relative frequency of carcinoma and the rarity of benign chronic peptic ulceration of the greater curvature.

Early figures, e.g., those of W. Brinton (1864), W. H. Welch (1885), and C. F. Martin (1909), quoting the incidence of peptic ulceration on the greater curvature as 2, 3·4, and 3 per cent, must nowadays be considered as far too high. This may be due, either to the fact that some of the characteristics of peptic ulceration have now changed, or to the fact that as a result of modern methods of diagnosis, especially the use of X rays, many more cases are seen and their true positions proved. E. S. Blaine (1925) stated that "many radiologists of great experience have never seen the condition".

H. Finsterer and K. Glaessner (1914) published a case of chronic peptic ulceration of the greater curvature with radiological and histological data, and reviewed the literature up to that time, but although they found 36 instances in which simple ulceration had been described, only 4 cases could be considered with assurance, and even in these the histological findings were not complete.

V. David (1928) reviewed the literature after 1914, and concluded that only 16 true cases of peptic ulceration of the greater curve had been described, and of these only 10 had been proved histologically.

W. B. Matthews (1935) reported 2 further cases, and, after searching the literature, concluded that only 22 cases of peptic ulcer of the greater curvature had been described in sufficient detail to warrant that diagnosis, and of these only 10 were proved histologically.

L. Popovie (1936) reported a further case which was almost identical with the case reported in 1914 by Finsterer and Glaessner.

J. Sproull (1935) pointed out that carcinoma occurring on the greater curvature may present both radiological and macroscopical appearances of benign ulceration.

The rarity of benign peptic ulceration of the greater curvature of the stomach may be contrasted with the figures of 4 and 6 per cent given respectively by A. J. Walton (1932) and R. T. Payne (1938) for the incidence of carcinoma occurring at this site. Whatever the cause for this difference in predilection, the fact should

be remembered when confronted with a case of ulceration on the greater curvature, and with this in mind we report the following case and some of the difficulties met with in diagnosis.

CASE REPORT

HISTORY.—L. R., female, aged 29 years, was admitted to the Sheffield Royal Infirmary on July 20, 1937, under the care of Mr. T. B. Mouat. She complained of pain in the epigastrium of nine months' duration. No indigestion was felt prior to the onset of pain. The pain occurred half an hour after meals, and was not relieved by food or alkalis. Occasionally pain persisted all day, and sometimes awoke the patient at night. There had been no

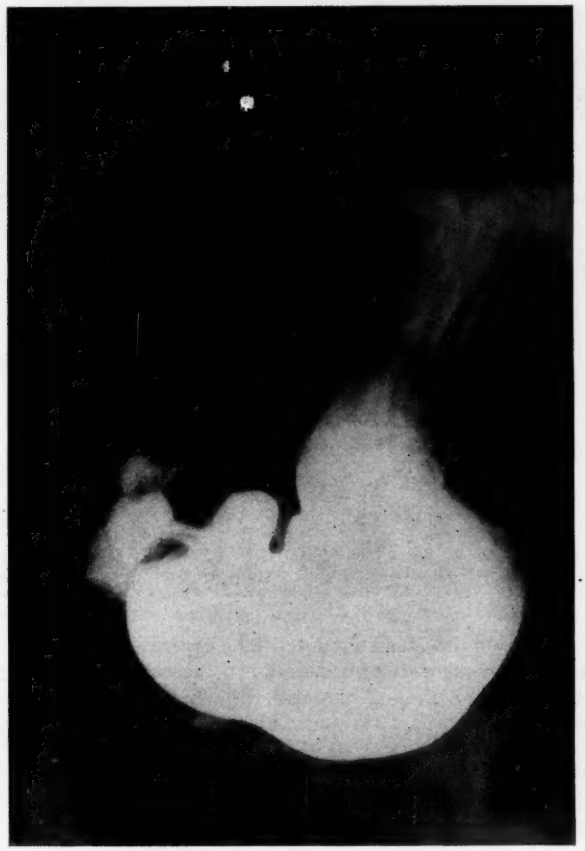


FIG. 225.—Radiograph of stomach, showing ulcer crater.

remissions from pain. The appetite was fair, but the patient was afraid to eat because pain followed. No nausea or vomiting occurred. The bowels were normal, there was no melæna, and micturition was normal. The menstrual history was normal. She had one child, aged 5 years. No miscarriages. Past and family history revealed no relevant data.

ON EXAMINATION.—The patient was a small, spare woman of fairly good colour. The teeth were good. Tenderness was present in the middle of the epigastrium and towards the left of the middle line. No tumour was palpable. Cardiovascular, pulmonary, and central nervous systems appeared normal. Hæmoglobin estimation 90 per cent. Blood group, II. Occult blood, negative. Blood W.R., negative.

Radiological Examination (*Fig.* 225).—The œsophagus was normal. The stomach was normal in size, tone, and position. Emptying began immediately. A small ulcer crater was detected

on the greater curvature of the stomach. The mucosal folds were thickened, and contraction towards the ulcer crater had occurred. The stomach wall around the ulcer was deformed, and its mobility and elasticity reduced. Emptying occurred readily; the prepyloric area and duodenum appeared normal. *Conclusions*: Ulcer on the greater curvature of the stomach, with no evidence of the cause.

Mr. T. B. Mouat resolved to treat the case as one of carcinoma of the stomach.

AT OPERATION (July 29, 1937).—The abdomen was opened under gas and oxygen inhalation anæsthesia, supplemented by local infiltration with 1–2000 percaine solution. An ulcer was found on the upper half of the greater curvature of the stomach. The stomach wall around the ulcer was thickened. The greater and lesser omenta, the transverse mesocolon, and the liver appeared normal. A high Polya type of gastrectomy was performed, and the ulcer included in the resected stomach. The jejunum was brought through the mesocolon and an anastomosis established.

HISTOLOGICAL REPORT (Dr. L. C. D. Hermitte).—When the stomach was opened after fixation in formalin, an ulcer was found on the greater curvature having all the appearances of a simple chronic gastric ulcer with slightly thickened edges and a fairly deep crater with fibrosis of the base, causing some puckering of the serous surface (*Fig.* 226).

A whole section passing through the centre of the ulcer transversely to the long axis of the stomach and including a large extent of mucosa of both anterior and posterior walls on either side of the ulcer showed the typical changes of a chronic gastric ulcer with a fibrous

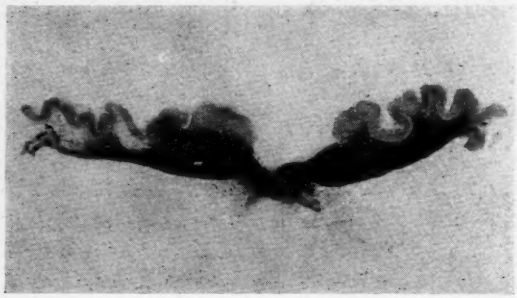


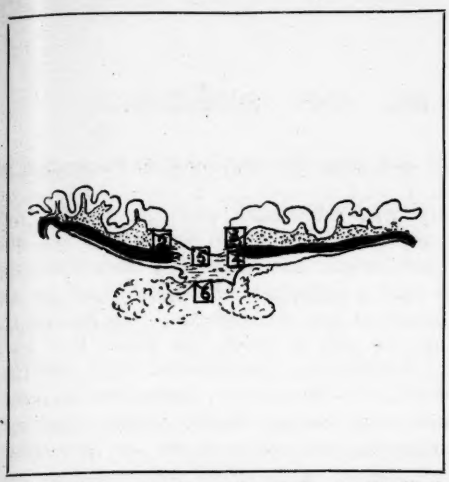
FIG. 226.—Section of stomach passing through middle of ulcer on greater curvature, showing simple chronic type, with slightly thickened edges and fairly deep crater.

floor covered with granulation tissue, surmounted by a layer of necrotic tissue (*Fig.* 227). The changes at the sides of the ulcer were undoubtedly suspicious, but—after careful consideration and taking into account: (1) the opinion of the two schools of thought regarding the question of malignancy developing on chronic ulcers in the stomach; (2) the fact that the hypertrophic gastritis in the immediate neighbourhood of the ulcer may be so marked as to lead to the expansion of the hypertrophied glands even to below the level of the muscularis mucosæ as well as leading to cystic dilatation; and (3) since the whole base of the ulcer had completely destroyed the muscle coat with replacement fibrosis and showed no evidence of malignant invasion—it was concluded that the lesion was purely a chronic gastric ulcer and that the abnormal appearance of the surrounding mucosa was compatible with it and due to hypertrophic gastritis.

However, a section was sent to Professor M. J. Stewart, of Leeds, who considered the lesion to be an ulcer carcinoma. Accordingly further sections were examined and the invasion of the submucosa proved more extensive than in the first section; and on re-examination of the latter it was admitted that malignant changes were indisputable, for there was actual invasion of the omentum attached to the stomach.

The slides were also submitted to Professor Dible, of the British Post-Graduate School, and a diagnosis of primary carcinoma was made.

Further slides were taken to Professor Stewart, who, after reviewing the histological findings and correlating these with the clinical data, considered that the weight of evidence was in favour of ulcerating primary carcinoma. The presence of an extensive complete breach in the muscular wall of the stomach, the breach being occupied by typical simple

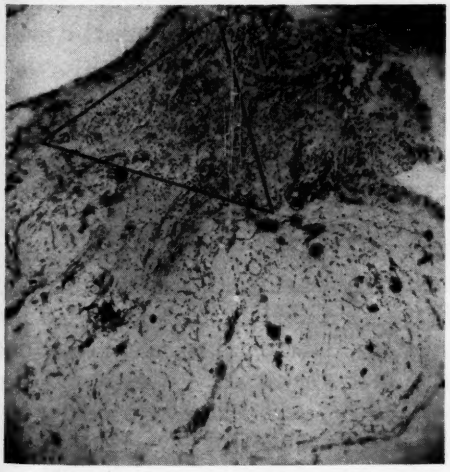


1, Outline drawing of whole longitudinal section of stomach wall passing through middle of ulcer, showing areas microphotographed. The numbers in the small squares correspond to those of the microphotographs.

2, Area at distal edge of ulcer showing (*a*) abnormal dilated glands in mucosa, (*b*) intact muscularis mucosæ, (*c*) a few malignant acini immediately below the muscularis mucosæ. The invasion of the submucosa on this side of the growth was nowhere deeper.

3, Area at proximal edge of ulcer, showing slightly more marked invasion of the submucosa by widely dilated malignant acini, fairly well differentiated and containing mucinous secretion.

4, Area of submucosa deep to last area (3), showing deeper invasion but by only a few scattered well-differentiated acini, indicated by arrows.



5, Area from omentum, showing early invasion of small well-differentiated glandular acini in black triangle. There is marked fibrous tissue reaction in the invaded area.

6, Area of floor of ulcer about its middle, showing the typical chronic inflammatory fibrosis of a chronic peptic ulcer, and complete absence of malignant invasion.

FIG. 227.—Histological examination of stomach wall passing through middle of ulcer.

chronic gastric-ulcer tissue, completely cancer-cell free, was the only change suggestive of ulcer carcinoma.

CONVALESCENCE.—The post-operative recovery was uneventful and the patient was discharged on August 14, 1937. On September 20, 1937, the patient stated that she was much improved. A test-meal examination was performed, and showed a very low total acidity curve, and absence of free hydrochloric acid. Unfortunately, these findings are rendered difficult to assess in view of the wide resection and anastomosis. On March 10, 1938, the patient was re-examined. She reported she had no pain, but could take only small meals. No gain in weight had occurred. Radiological examination disclosed that three ounces of barium suspension filled the stomach to the cardiac orifice in the erect position. Emptying occurred readily. The stomach pouch was elastic and regular of outline. On December 1, 1938, the patient reported that she was very well and had no discomfort.

Comment.—This case shows clearly the limitations of scientific investigation, and emphasizes the necessity for correlation of facts and attention to detail. Clinical features were indefinite. Radiological examination indicated the situation, but not the nature of the ulceration. The short history, together with the unusual situation of the ulceration, suggested the probability of carcinoma, and determined the course of treatment. At operation the findings suggested neoplastic change, but macroscopical examination of the excised specimen was inconclusive. The first histological examination led to a diagnosis of simple ulcer, but further sections disclosed undisputed carcinoma. It is unfortunate that a pre-operative test-meal was omitted, for this might have furnished a clue to the chemical environment in which the growth began. Some of the features suggest ulcer-carcinoma, but the consensus of opinion is in favour of a primary carcinoma.

DISCUSSION

The problem of the nature of ulceration on the greater curvature is especially difficult, because the cases met with are few and may be atypical. Investigations must be conducted in an orderly manner, with correlation of the facts ascertained from clinical, laboratory, and radiological data. It is recognized that no characteristic clinical features are known, and that frequently opinions given from radiological examinations have been incorrect.

In the case reported by J. Sproull, the radiographical appearances were interpreted as those of peptic ulcer. At subsequent examinations it was found that the crater did not heal or progress in size. The ulcer was removed by local resection. It appeared simple on examination, but histologically was carcinomatous. Two years later a recurrence was found at operation, with secondary invasions of the lymph-glands.

W. B. Matthews (1935) described two cases in which the radiological opinion was given as neoplastic, but which were found to be simple on histological examination.

At Vichy, before the Society of Electrology and Radiology, E. and S. Dechambre showed a case of ulceration of the greater curvature and attributed the aetiology to syphilis. They stated that radiology would not permit an opinion upon the nature, but only upon the existence and situation, of the ulceration. This is borne out by the two cases reported by V. David (1928), one of which resulted from swallowing corrosive solution and the other was a local manifestation of aleukæmic lymphadenosis. F. G. Ralphs (1938) states that he had seen a case of ulceration of the greater curvature due to chronic inflammation resembling that described by Crohn as occurring more commonly in the ileum.

The radiographical appearances must be interpreted in terms of anatomy and pathology, in accordance with the researches of G. Forssell (1913) in gastric ulcer. When a deformity is seen, its exact nature must be ascertained, or the ulcer may be missed. The size of the ulcer varies. Enormous simple ulcers have been

described by Finsterer and Glaessner, and by Popovie in which the crater penetrated the spleen. With peptic ulceration, the mucosa around it may be irregularly swollen, as well as drawn towards the crater. A wide area of diminished mobility and elasticity of the stomach wall may be present.

A. E. Barclay has seen cases in which the lesser curvature was drawn across to a fixed point on the greater curvature. A functional ' hour-glass ' stomach was present, with the opening towards the outer side.

F. Kuhlmann in 1934, at the 25th Congress of the German Roentgen Society, demonstrated the radiographs of two cases of ulceration of the greater curvature, in which the diagnosis and subsequent complete healing had been verified by gastroscopy. He described a transverse fold of the stomach wall which crossed the stomach towards the ulcer crater, and above which the barium tended to collect. In another case of malignant ulcer this feature was not present.

A crater may be simulated by a mucosal pocket in an area of hypertrophic gastritis, a gastric diverticulum, or on cursory examination by lesions of the duodeno-jejunal loop. In hypertrophic gastritis, a single pocket amid swollen rugæ is like a small ulcer, but the involved wall is elastic and mobile, and there is no evidence of retraction by fibrosis. Gastric diverticula along the greater curvature are uncommon. The adjacent stomach wall is normal, unless secondary changes are present.

Deformity of the greater curvature of the stomach may be caused by ulcers on the anterior or posterior wall, if situated towards the left. Accurate localization of the crater is essential.

The appearances of simple peptic ulceration may be given by neoplasm. Sproull's case clearly demonstrates this point. Prior to seeing the case reported here, some radiographs were shown to one of us by Dr. Lohmann, of Berlin, in which the features were similar, and the histological findings carcinomatous.

Gastroscopy is now available to aid in diagnosis and to assess the results of treatment, but N. Henning (1935) states that although the gastroscopic diagnosis in well-marked cases of carcinoma is easy, in some cases only histological section can decide the problem.

It has been stated by Matthews that there is no certain method for the differentiation of the cause of ulcer of the greater curvature except by histology. He concludes that all ulcers of the greater curvature should be treated surgically. The problem is similar to that of the prepyloric ulcer, when clinical signs and the analysis of gastric contents are often inconclusive. In these cases, it is not possible to diagnose a simple ulcer at a single radiological examination.

If it is decided to withhold surgical treatment, the patient should be placed on a strict medical régime. When the ulcer is simple, pain becomes easier, tenderness less marked, and occult blood disappears from the stools. At radiological examination, spasm disappears, the ulcer crater becomes shallower, and the mucosal edges tend to subside. Re-examination should be made after one week's interval. When definite improvement is demonstrated, medical treatment can be continued, controlled by further examinations of the stomach until the ulcer is healed completely. Control is facilitated if gastroscopic examinations can be made to ensure that progress to complete healing takes place, but symptomatic improvement and apparent radiological diminution of the ulcer crater may also occur in neoplasm. J. Morley has published an excellent series of radiographs which show clearly how

an ulcer niche may be diminished in size, the picture masking unsuspected growth.

In the light of present knowledge, early surgical intervention appears justifiable. R. Maingot has expressed the opinion that a chronic ulcer situated on, or within half an inch of, the greater curvature, even although it possesses the radiological features of a simple ulcer, should be regarded and treated as neoplastic.

When surgical exploration is undertaken, a wide resection in the form of a partial gastrectomy is necessary, even if the macroscopical appearances are those of a simple lesion. Technical difficulties may be met with, because a high type of gastrectomy may be needed. Proximity to the spleen may necessitate splenectomy. A sufficient margin at the cardiac end of the stomach must be allowed to perform a safe anastomosis, and the left coronary ligament of the liver and even the costal margin may need division to attain proper access.

SUMMARY

1. A case of chronic ulceration of the greater curvature of the stomach is described.

2. The difficulties met with in diagnosis are considered, and it is concluded that it is impossible to exclude the presence of neoplastic change unless it can be shown that progressive and complete healing follows medical treatment.

3. When the healing does not occur, is delayed, or doubtful, then a wide surgical resection in the form of a partial gastrectomy is advised.

The writers are indebted to Mr. T. B. Mouat for his help and permission to record this case, and to Dr. J. Wilkie and Dr. L. C. D. Hermitte for the services of their departments.

We are especially grateful for opinions and advice given by Dr. A. E. Barclay, Professor Dible, Mr. R. T. Payne, Professor M. J. Stewart, and Professor Grey Turner.

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THE BENIGN FIBRO-OSSEOUS TUMOURS OF THE SKULL AND FACIAL BONES

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THERE occur in the bones of the skull and face a group of benign tumours, produced by the transformation of fibrous tissue directly into bone by metaplasia. Because of this structural similarity, and in spite of wide variations in their clinical and gross pathological features, it is justifiable to consider them together. They range from the ossifying fibromas of the jaws, which contain only small amounts of bone and were formerly regarded as pure fibromas, to the mature bony compact osteomas, and include many varieties of intermediate hyperostoses, frequently described as focal osteitis fibrosa.

Confusion has arisen in the past by the failure to differentiate these tumours from the osteochondromas found elsewhere in the body, and the generalized skeletal diseases of osteitis deformans and osteitis fibrosa cystica. The purpose of this study is to enumerate the chief types of tumours in this group, emphasizing their pathological inter-relationship rather than to consider in great detail their clinical features and possible complications.

During the course of development of these tumours, the whole cycle of ossification in membrane may be reproduced, and, unlike the osteochondromas, cartilage is never present. It is, therefore, not surprising to find that they are limited to those cranial and facial bones which are ossified in membrane. Only small parts of the maxilla and mandible are ossified in cartilage, and although osteochondromas do rarely arise here, the majority of osteomas of these bones are fibrous in origin. In addition the zygomatic, nasal, vomer, and lacrimal bones of the face, and the frontal, parietal, squamous temporal, the great wings of the sphenoid, the occipital bones above the nuchal lines, and the tympanic plates of the skull, are purely membranous in origin and are therefore liable to develop these tumours, while the cartilage-containing osteomas are found in the bones of the base of the skull.

The skull grows rapidly from birth, until the seventh year of life, and subsequently more slowly until puberty, when there is a rapid increase in the rate of growth, especially in the frontal and facial regions, coincident with the development of the accessory nasal air sinuses. The occurrence of these fibro-osseous tumours in children and young adults, singly or in several foci, most commonly in the later developing frontal and facial bones as Echlin (1934) has pointed out, suggests a growth disturbance, and this view is supported by their usual origin in the actively growing periosteal or subperiosteal regions, and their tendency to stop growing in later life.

TYPES OF FIBRO-OSSEOUS TUMOURS

Four main types of these tumours will be described: the ossifying fibromas; the fibrous or spongy osteomas limited to a part or whole of one bone; the localized compact osteomas; and the diffuse osteomas or hyperostoses occupying several adjacent bones.

THE OSSIFYING FIBROMAS

In the older text-books on diseases of the jaws, such as those of Heath (1894) and Scudder (1912), there are good descriptions of fibromas of the jaw, and calcification and ossification within their substance is mentioned as being a frequent finding, but without much comment. Many of these tumours have been excised in mistake for sarcomas and are present in the medical museums labelled fibrosarcomas, but the true fibrosarcomas are not bone-forming and are not composed of mature fibrous tissue. Montgomery (1927) described three fibromas of the jaw showing various amounts of ossification within their substance, collected a further fourteen examples from the literature, and termed them ossifying fibromas. Phemister and Grimson (1937) later included these cases in a more extensive series, pointed out the transition between these tumours and the osteomas of the jaws, and suggested the common title of fibrous osteoma.

FIG. 228.—A central ossifying fibroma removed together with a portion of the horizontal ramus of the mandible. The surface of the tumour is covered by a thin shell of new bone. A tooth is embedded in the substance of the tumour. (*Specimen No. 4AF9, University College Hospital Museum.*)

The ossifying fibromas occur in either sex, in children and young adults. Geschickter and Copeland (1936) found that just over two-thirds of a series of thirty ossifying fibromas arose in patients under thirty years of age. They are usually painless and grow slowly for a number of years before the deformity is noticed by the patient, but occasionally obstructive symptoms may develop if the expansion encroaches upon the orbit, causing proptosis and diplopia; or blocks the lacrimal duct or nose, producing epiphora or nasal obstruction and epistaxis. The commonest sites are in the horizontal ramus of the mandible and in the walls of the antra, but fibromatous types of osteomas are found in the vault of the skull, which are similar in structure. Multiple ossifying fibromas of the jaws occasionally occur and have been described by Dolamore (1920) and Phemister and Grimson (1937). There is a striking association with carious teeth and occasionally with trauma in the published cases.

I have examined histologically three specimens in the museum of University College Hospital, Nos. 4AF8, 4AF9, and 4AF10, which illustrate the characters of the tumours in the horizontal ramus of the mandible. They appear to be central in origin, and to expand the jaw as they grow (*Fig.* 228), but the thin shell of bone which covers the surface of the tumour is in fact new subperiosteal bone and blends with the fibro-osseous stroma of the tumour without the separation of a true capsule. They are probably not, therefore, truly central, but arise subperiosteally and grow into the jaw. The ascending ramus of the jaw usually remains unaltered, and the tumour is confined within the substance of the horizontal ramus, but in one case, No. 4AF8, the tumour reached an enormous size, and grew out of the alveolar margin into the mouth. The specimen was removed by Mr. Liston

from a man aged 30 years who had noticed a swelling in the right lower jaw for two-and-a-half years. The horizontal ramus of the jaw in the specimen is replaced by a large pink fibrous tumour, covered by a thin shell of bone, except where it has grown upwards into the mouth for a distance of 10 cm. to form a lobulated

FIG. 229.—Radiograph of a specimen showing replacement of the substance of the horizontal ramus of the mandible by a tumour which has grown out of the alveolar border. There are numerous spicules of bones and masses of calcification in its substance. (*Specimen No. 4AF8, University College Hospital Museum.*)

fibrous and gritty tumour. A radiograph (*Fig.* 229) shows a translucent tumour surrounded by a thin shell of bone in its lower half only, and full of small bony trabeculæ and flecks of calcification.

FIG. 230.—*Case* 1. Radiograph showing obliteration of the right antrum by the tumour. The substance is irregularly mottled and the margin outlined by a thin layer of sclerosed bone.

The following case illustrates the type of tumour which occurs in the upper jaw.

Case 1.—A woman of 31 years was admitted complaining of a painless swelling of the right cheek. Three years ago a simple fibroma had been scraped out of the right antrum through the mouth. There was a firm swelling of the maxilla, which bulged the cheek outwards and expanded the right alveolus into the mouth. It extended up as far as the floor of the orbit without displacing the eye, laterally as far as the zygoma, and medially narrowed the lateral nasal canal. A radiograph (*Fig.* 230) showed obliteration of the antrum by an irregularly mottled, mainly translucent tumour with a sclerosed margin. It was thought to be a sarcoma, and Mr. M. Formby therefore excised the right upper jaw, leaving the floor of the orbit intact. An obturator was fitted and the patient has remained free from recurrence for three years.

FIG. 231.—*Case* 1. The right upper jaw, which was excised at operation. Note the expansion of the alveolar margin and the outgrowth of the tumour on the buccal aspect.

Examination of the specimen (*Fig.* 231) reveals a soft fibrous tumour almost completely replacing the maxilla and obliterating the antrum. The maxilla is enlarged in every direction, except posteriorly, and on the buccal aspect it is forming a dome-shaped swelling, covered by a thin shell of new bone. Elsewhere the edge is ill-defined, and blends with the surrounding bone. The zygoma is not involved. The tumour cuts readily with a knife, but the surface is gritty and speckled with calcified particles. The tooth roots are embedded in the substance of the tumour and appear healthy, but the second molar tooth is missing.

Through the kindness of Mr. E. D. Davis I have seen a further very similar example of the disease in the upper jaw. A woman of 34 years had a benign tumour removed from the left upper jaw eight years previously, and this had slowly recurred. On examination, there was a firm painless enlargement of the left maxilla, and the radiograph showed an almost identical picture to that in the last case. The swelling was explored through the alveolus and a tough fibrous tumour found projecting into the antrum. The tumour was scraped out and the wound allowed to granulate.

The histological structure of these five tumours is similar. They are composed of mature fibrous tissue with scattered areas of calcification and ossification within their substance and well-developed blood-vessels. In parts the fibrous tissue is coarse, there are numerous interlacing bundles of stout collagen fibres, relatively few cells, and little or no ossification. In other areas the tissue is much more cellular, with fewer fibres and active bone formation (*Fig.* 232). There are sometimes also myxomatous areas (*Fig.* 233) where the cells are stellate in form and widely separated, and a few small cysts are present. The new bone is of the woven fibrous variety and stains deeply with hæmatoxylin, shows no laminations, and can be seen to be fibrous in structure. The cells in the vicinity are plumper and in places are arranged in rows adjacent to the trabeculæ where they are acting as osteoblasts. In other places the new bone is being eroded by osteoclasts lying in large bays or Howship's lacunæ.

Another characteristic of these tumours is the calcification which is present in the form of spherical calcium concretions (*Fig.* 234). They have been observed by several writers—Dolamore (1920), Lawford Knaggs (1926), Geschickter and Copeland (1936), and Trauner (1939)—in the benign tumours of the membrane

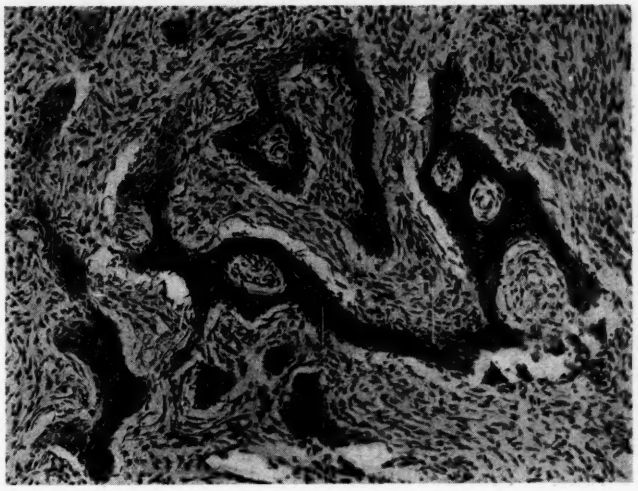

FIG. 232.—Low-power view of a section of an ossifying fibroma of the mandible. Trabeculæ of woven bone are being laid down and actively eroded by osteoclasts. The fibrous tissue is richly cellular. (H. and E.) (× 65.)

bones of the skull and face. They are laid down in the fibrous tissue on a basis of hyaline substance which stains pink with eosin and can often be seen as a narrow zone around the circumference. They stain pale blue with hæmatoxylin in the centre and darker blue in the outer rings and contain no cells, either within

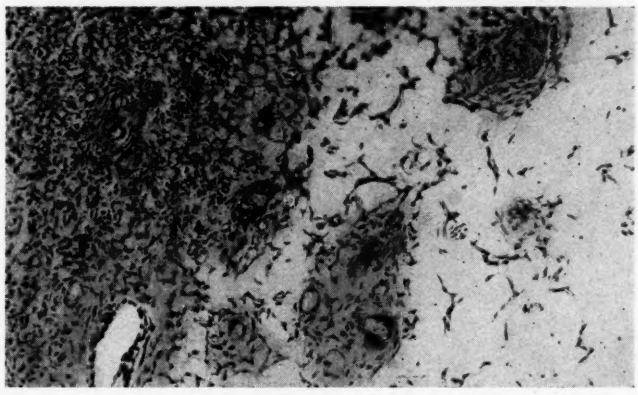

FIG. 233.—*Case* 1. Low-power view of a myxomatous portion of the tumour. On the left the fibrous tissue is more cellular and a few calcium spheroids are beginning to form. (H. and E.) (× 65.)

their substance or around their periphery. Adjacent concretions run together to form trabeculæ, in which the ring structure may be partially preserved, and all stages of transition can be traced up to true bone. Sometimes they are incorporated whole and unchanged into the substance of mature bone (*Fig.* 235). They are most frequent where bone formation is active, and are found not only in these

tumours, but in the fibrous epulis and in the spongy osteomas of the skull and face. In addition, I have found them in the section of bone from the upper jaw in a case of generalized osteitis deformans with facial involvement (*Fig.* 236).

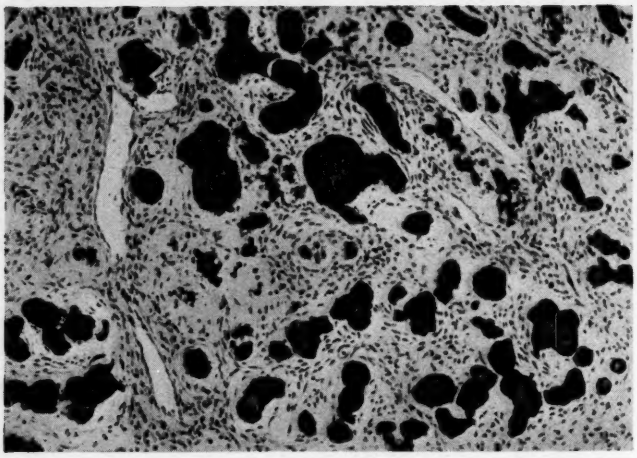

FIG. 234.—*Case* 1. Low-power view showing the general appearance of the tumour. Numerous calcium spheroids are lying in a stroma of cellular fibrous tissue. In places they are running together to form trabeculæ, but there are no cells within their substance or around their circumference. (H. and E.) (× 65.)

Superficially they resemble the psammoma bodies of the dura and meningiomas, but their ring structure is not due, as in those tumours, to calcification of concentric rings of hyalinized cells and fibres. Lawford Knaggs (1926) thought they might represent deposits of excess calcium derived from the active destruction of bone,

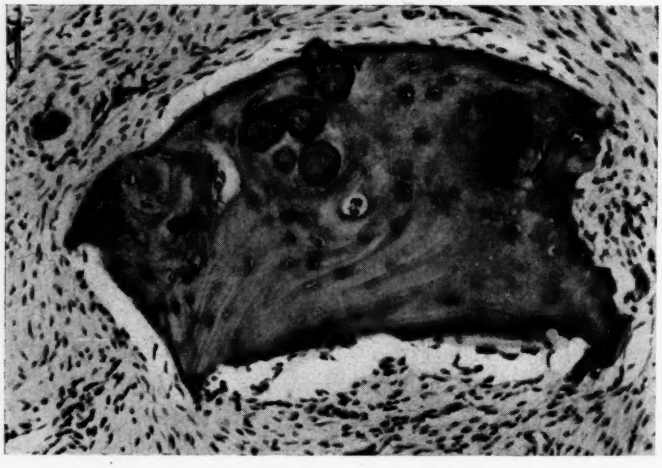

FIG. 235.—A trabecula of bone in the substance of a fibrous epulis. It consists of laminated bone but within the substance are several intact calcium spheroids. (H. and E.) (× 115.)

but this explanation is unlikely in view of their frequency in the fibrous epulis where there is practically no destruction of old bone. It would seem more likely that these calcium spheroids represent some derangement of early bone formation in membrane, whereby the calcium is deposited in globular masses independently of the cellular mechanism of ossification.

Although the fibrous epulis is usually considered along with other tumours of the gums, the similarity of its histological structure to the central fibroma of the jaw necessitates its inclusion in this study. Pure fibromas of neurogenic origin showing palisading of cells have been described by Thoma (1938), and simple

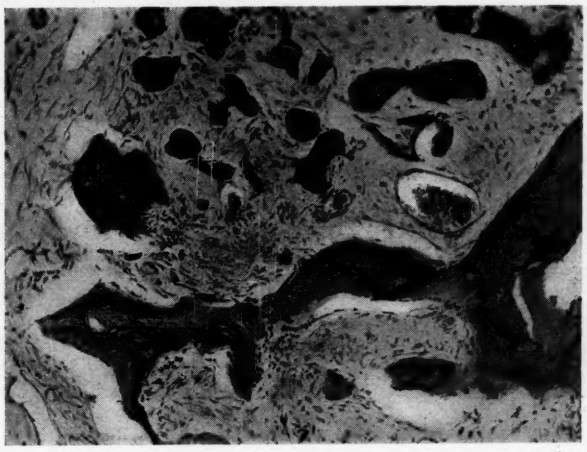

FIG. 236.—Low-power view of a section of bone from the upper jaw in a case of generalized osteitis deformans. There are trabeculæ of young woven bone which are being actively remodelled. Above are several calcium spheroids, one incorporated within the substance of a trabecula. On the right are two calcium spheroids running together to form a trabecula of primitive bone and containing a few swollen cells. (H. and E.) (× 65.)

fibromas occur in this vicinity in addition to the tongue and lips and other parts of the mouth. A common form, however, is a fibro-osseous tumour arising from the periosteal region of the alveolar margin or the depths of a tooth socket. It occurs in either jaw in children and young adults in association with carious teeth, most frequently but not invariably in the canine region. As the tumour grows it loosens and displaces the teeth, and forms a mushroom-like swelling interfering with mastication (*Fig.* 237). A tumour in the museum of University College Hospital, No. 4AF4, shows the size which may be reached. This specimen measures 6 cm. in its greatest diameter and hung down from the upper jaw as far as the lower border of the mandible.

FIG. 237.—A large fibro-osseous epulis.

The histological structure of the fibro-osseous epulis is essentially similar to that of the central fibroma, and calcium concretions and spicules of bone are found in the more cellular areas of fibrous tissue. The surface, however, is not covered by a shell of periosteal bone, but lies directly under the mucous membrane of the gum, and deep branching processes of squamous epithelium pass into its stroma. It lies on the surface of the alveolus and around the tooth roots, and the fibrous tissue blends imperceptibly with the adjacent periosteum. Round-celled infiltration is frequent, and there may be areas

of superficial ulceration. It must, therefore, be considered as a fibro-osseous overgrowth of the alveolar dental periosteum.

Although it is uncommon to find ossifying fibromas of the skull bones, there is a variety of tumour usually classed as an osteoma or an area of focal osteitis fibrosa which appears very similar in structure to the ossifying fibromas of the jaws.

Case 2.—A woman of 41 years had suffered from major attacks of epilepsy since the age of 15. For about the same time she had had a painless swelling of the forehead, which had grown slowly during adolescence and was now stationary. There were no neurological

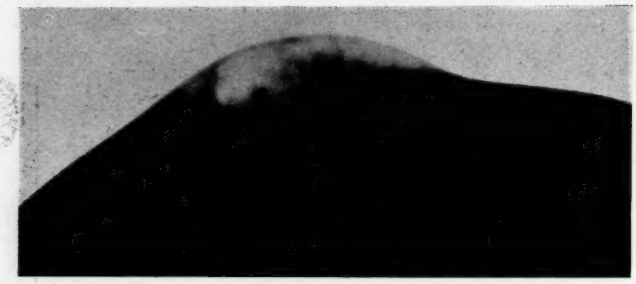

FIG. 238.—*Case* 2. A radiograph of the tumour of the frontal bone. The outer table of bone has disappeared, the inner table remains unaltered, and the tumour appears as a translucent cyst-like swelling continuous with the diploe. The outer surface is well defined and covered by a thin shell of bone, and there are mottled opacities within its substance.

signs; the swelling was smooth and dome-shaped, measuring $2\frac{1}{2} \times 2$ in., and lay just in front of the coronal suture in the middle of the frontal bone. A radiograph (*Fig.* 238) showed a translucent swelling containing mottled opacities projecting out of the frontal bone, resting on an intact inner table and covered by a thin layer of bone on its outer surface.

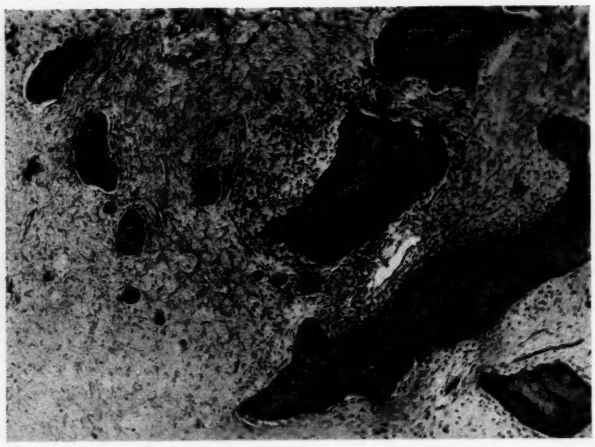

FIG. 239.—*Case* 2. Low-power view of the tumour to show the richly cellular fibrous stroma containing scattered calcium spheroids and trabeculæ of primitive blue-staining bone. (H. and E.) (× 65.)

At operation, Mr. Harvey Jackson excised the tumour in the centre of an osteoplastic flap. The underlying brain and inner table were normal. The swelling was, therefore, shaved off with a knife, the contents scooped out, and the inner table replaced in position. The epilepsy was unaffected. The surface of the tumour was covered by periosteum and a thin layer of subperiosteal bone, but the remainder of the substance was dense fibrous tissue full of gritty particles and blended with the surrounding diploe.

The sections of this tumour (*Fig.* 239) resemble those of the jaw tumours, and show many calcium spheroids and slender short trabeculæ of primitive woven bone scattered through a fibrous tissue stroma.

The ossifying fibromas, therefore, represent the most immature form of benign fibro-osseous tumour of the membrane bones. They tend to arise early in life, frequently in association with infected teeth, to grow rather more rapidly than the osseous forms, and to recur if incompletely removed. There may be difficulty in distinguishing them from malignant growths, and when the diagnosis is in any doubt a preliminary biopsy is desirable, which may be carried out together with the extraction of carious teeth. In the jaws the radiographic appearance is sometimes confused with that of an adamantinoma or osteoclastoma. As a rule, however, the central fibroma does not form a multilocular cyst, and the calcification is irregular and in the form of flecks scattered within its substance rather than true trabeculation.

THE LOCALIZED FIBROUS OSTEOMAS

The localized osteomas are of two main types, the fibrous osteomas, which are ill-defined spongy tumours often occupying the whole of one bone, and the compact osteomas, which are hard button-like swellings of mature bone arising from one surface. These two types are found anywhere in the membrane bones of the skull and face, but most commonly in the frontal and facial regions. Thoma (1934) distinguished the circumscribed true benign osteomas from the hyperostoses, which he described as diffuse enlargements of a bone or part of a bone, but he later confessed that the distinction was difficult and frequently a matter of opinion. Geschickter and Copeland (1936) found in a series of these tumours that 30 were in the upper jaw, 19 antral or intranasal, 21 in the lower jaw, 4 in the frontal sinuses, 2 intra-orbital, 9 on the external surface of the frontal bone, 1 mastoid, and 1 occipital.

One of the earliest descriptions of the fibrous osteomas was given by Westmacott (1913). He described them as they occur in the maxilla under the title of chronic hyperplasia of the superior maxilla, because of their ill-defined nature and tendency to involve the whole bone. Lawford Knaggs (1926) later described cases of this type as localized osteitis fibrosa, and pointed out a relationship to infected teeth. Echlin (1934) has more recently described the characters of these tumours in the skull, and Phemister and Grimson (1937) the jaw tumours. Trauner (1939) has given a very full and detailed account of their pathological features which he has studied in excised specimens.

They occur equally in the sexes, are sometimes multiple, but usually single, and arise, as a rule, in the first half of life. Of 10 cases in my records, of which 5 were maxillary, 2 frontal, 2 mandibular, and 1 temporal and occipital, the average age of onset was 17 years. The history is of a benign, slow-growing tumour which is painless and causes no symptoms until it becomes disfiguring or produces pressure effects. When it is allowed to reach large dimensions, there may be hideous deformity, proptosis of the eyes, obstruction of the lacrimal canal or nose, or headaches and epileptic fits. There is a general tendency, however, to grow in the line of least resistance, i.e., into the mouth or cheek or on to the surface of the skull.

The maxilla appears to be the commonest site, and the whole bone is usually involved by the growth, the canine fossa obliterated, the alveolus enlarged, and

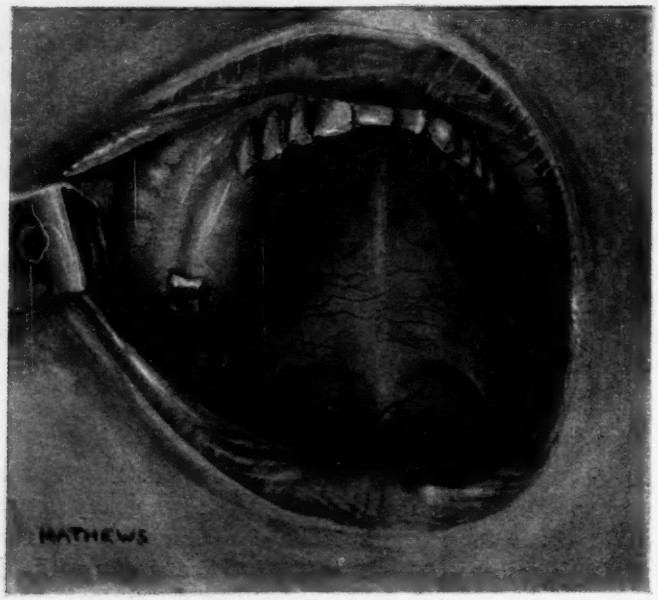

FIG. 240.—*Case* 3. The appearance of the tumour from within the mouth. The right upper first and second molar teeth have been extracted. The swelling is confined mainly to the premolar and molar regions.

the lip and cheek pushed out by the swelling. The inferior orbital margin is sometimes thickened, and the antrum filled up with new spongy bone, but the nose is not generally invaded. Worth (1937 and 1939) has described three different types of radiographic appearances of these tumours, two of which are maxillary forms; the first occurs in young subjects and gives the appearance of the outer surface of the rind of an orange, and the second,

FIG. 241.—*Case* 3. Radiograph of the right upper jaw. The antrum is obliterated by a spongy osteoma, the outer surface of which is well defined by a thin layer of new bone.

in adults of any age, forms a dense structureless mass of new bone. His third type is the mandibular form, and produces an ill-defined swelling with a ground-glass appearance, or irregular calcification surrounding small cyst-like cavities. Infection in the form of carious teeth or sinusitis is a frequent complication of both types. The following case illustrates the disease as it is found in the upper jaw.

Case 3.—A youth of 19 years complained of a painless swelling of the right cheek for five years. There was no general disease, but the right cheek was rendered prominent by a swelling of the maxilla extending up as far as the inferior orbital margin, and causing bony enlargement of the right upper alveolar margin and mouth, especially in the molar and premolar regions (*Fig.* 240). The first two molar teeth on that side were carious. Radiographs of the skeleton were normal except that in the right maxilla there was an opacity completely obliterating the antrum and projecting into the cheek (*Fig.* 241). The outer edge of the swelling was well defined as a thin layer of cortical bone, and the substance was irregularly mottled with areas of sclerosis and rarefaction. The blood-calcium was 9·2 mg., and the phosphorus 2·8 mg. A biopsy was performed through the mouth, and after penetrating the thin outer shell of bone, soft spongy vascular bone was encountered. The carious teeth were extracted, and the swelling has remained unchanged for three years.

In the lower jaw the tumour seldom involves the whole bone. It is most frequently found in the horizontal ramus and forms an ill-defined swelling which merges with the normal bone. The following case is an example of this type.

Case 4.—A girl of 16 years complained of a swelling of the right lower jaw for two years, which had been getting steadily bigger, was only slightly painful at times, but was beginning to interfere with speech and mastication. There was no general disease, but the right lower jaw appeared unduly prominent, and there was a diffuse swelling extending from the middle line in front to the region of the angle of the jaw. It was hard, and only slightly tender, and was most marked on the outer side of the jaw. The teeth were healthy, but the last molar tooth was unerupted. A radiograph of the jaw (*Fig.* 242) showed an ill-defined area of sclerosis with patchy rarefaction in the middle of the horizontal ramus, causing slight expansion of the jaw, but with no abscess or sequestrum. The remainder of the skeleton was normal. The blood-calcium was 10·5 mg., and the phosphorus 5·2 mg. A biopsy was performed through the mouth, and showed the tumour to consist of vascular spongy bone, covered by a thin shell of cortical bone. No pus was found, and the culture was sterile. The swelling has remained unchanged for four years.

FIG. 242.—*Case* 4. Radiograph of the right lower jaw to show the ill defined mottled opacity in the centre of the horizontal ramus.

The same type of tumour is found in the membrane bones of the skull, and may project either outwards under the scalp or occasionally into the cranial cavity, causing cortical irritation. The outer surface is covered by periosteum and a thin shell of cortical bone, which is seen in the radiograph to be continuous with the adjacent outer table. The substance is composed of fine, spongy, new bone, passing into the diploe, and the whole or part of the bone may be expanded with obscuring of the normal separation between cortical and cancellous bone. The opposite inner table of the bone is frequently unaffected or slightly thickened and depressed.

Like the corresponding tumours of the jaw, the fibrous osteomas of the skull arise early in life, grow slowly for many years, and then become stationary. A history of trauma sometimes precedes the appearance of the tumour. The frontal

bones are most commonly affected, and the supra-orbital ridges may be thickened, the frontal sinuses obliterated, or the eyes displaced. There have been two examples of multiple tumours of the skull in this series, one of which was reported by Taylor (1935), and the other is described fully below.

Case 5.—A girl of 19 years was admitted complaining of two painless swellings of the head, which had appeared several years previously and were getting steadily bigger. She was a healthy subject, with no evidence of disease except the two tumours, one just in front of the right ear, and one on the back of the head. On examination they were ill-defined bony projections from the skull, each measuring approximately 4 × 5 cm., and covered by soft lobulated tumours which felt like lipomas. Radiographs of the rest of the skeleton were normal. The osteomas were similar in type, one arising from the squamous occipital bone, and one from the right squamous temporal bone. They formed dome-shaped swellings, with sharply defined outer surfaces, and blended at their bases with the diploe of the underlying bones. The outer table in each case had completely disappeared, except at the edges, where it was continued on to the surface of the tumours; the inner table in each case was unaffected. (*Fig.* 243.)

FIG. 243.—*Case* 5. Radiograph of the osteoma of the occipital bone. The tumour is well defined and its substance spongy in appearance. At its base it blends with the substance of the underlying bone with replacement of the outer table. The inner table is intact.

The two tumours were operated on at different times by Mr. Wilfred Trotter, and found to be covered by lipomas attached firmly to their surfaces. The lipomas were removed, and the osteomas, composed of spongy new bone, cut off at their bases.

The patient was not seen again until seven years after discharge, when she returned complaining that the swellings had recurred. On examination, in addition to the two tumours which had grown again, there were several more small ones scattered over the vault of the skull. No further treatment has been given to date.

The histology of these tumours is similar in all situations. The outer surface is covered by a layer of fibrous periosteum, overlying a thin shell of cortical bone composed of fairly mature new laminated bone, laid down in trabeculæ parallel to the surface and separated by a little fibrous tissue (*Fig.* 244). Below this, the trabeculæ are slender, pass in all directions, and are separated more widely by the fibrous stroma (*Fig.* 245). This bone is less mature, mainly of the woven blue-staining type, and shows evidence of extensive remodelling. Where the stroma is richly cellular bone formation is active and occasional calcium spheroids are present. In other areas where the cells are fewer and the fibres coarser and more plentiful bone formation is less active, and wide tracts of fibrous tissue devoid of

ossification are found. At the base the tumour passes indefinitely to a variable depth into the normal cancellous bone beneath. It appears, therefore, that these tumours are usually subperiosteal in origin.

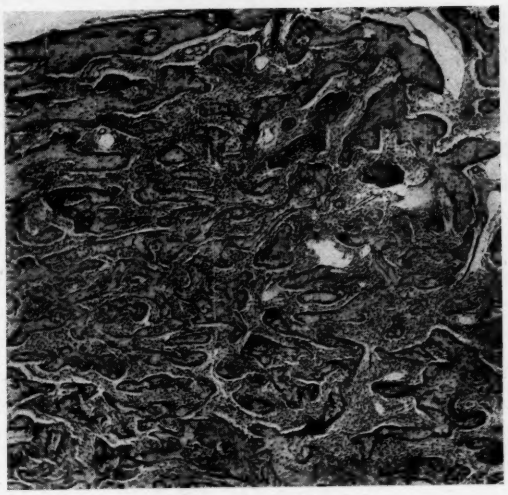

FIG. 244.—Low-power view of a section of a fibrous osteoma. In the top left-hand corner is the outer surface of the tumour covered by a thin layer of fibrous periosteum and trabeculæ of laminated bone, parallel to the surface, with small haversian systems. Deeper down the bone is more primitive, the trabeculæ run in all directions, and the fibrous tissue is more plentiful. (H. and E.) (× 25.)

It is important to distinguish the hyperostoses caused by the infiltration of the skull bones by cerebral meningiomas. Much has been written about these tumours, i.e., Taylor (1928), Echlin (1934), and Rowbotham (1939), and their differentiation

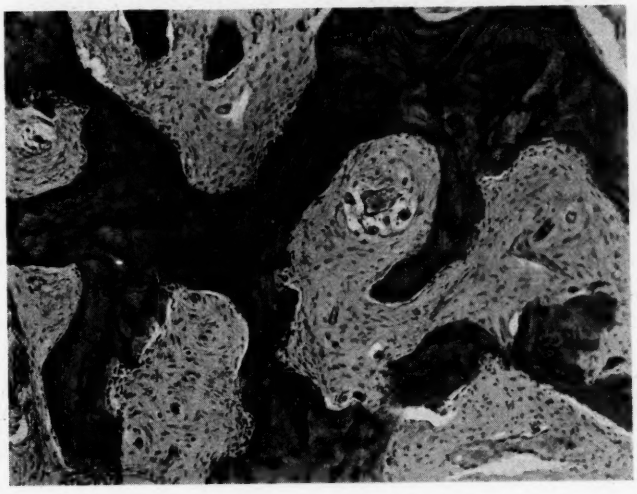

FIG. 245.—Section of a small portion of a fibrous osteoma to show the primitive bone with evidence of extensive remodelling. (H. and E.) (× 65.)

from the osteomas is often difficult. They arise later in life, grow faster, and are more frequently associated with nervous signs. Radiologically they usually show, in addition to increased vasculature of the diploe, new bone laid down at first

parallel to the intact inner and outer tables, and later, when the periosteum is broken through on the outer side, in sun-ray spicule formation. An uncommon tumour which is also a cause of confusion is the bone angioma, which, however, is highly characteristic radiologically and produces a 'sunburst' appearance, with alternate radiating streaks of sclerosis and rarefaction from a central focus. Sarcomas of the vault of the skull are rare, but occur in the jaws, and, like the infiltrating carcinomas, grow more rapidly, are frequently painful, and produce extensive destruction of the bone. Deposits of lipoid granuloma and secondary carcinoma in the skull look like punched-out holes in the radiograph, and dermoid cysts produce clear-cut defects with slightly sclerosed margins and are not likely to be confused with the osteomas.

THE LOCALIZED COMPACT OSTEOMAS

The compact or ivory osteomas are small dome-shaped tumours of very hard mature bone, which are found all over the membrane bones of the skull and face, on either table of the mandible along the alveolar margins, on the hard palate and surface of the zygoma and maxilla, on either table of the bones of the vault of the skull, frequently in the external auditory meatus and orbit, and in the antra and frontal sinuses. The osteomas of the sinuses form a special group

FIG. 246.—Compact osteoma of the right occipital bone. Note the limpet-like appearance, and the polished summit with numerous vascular foramina nearer the base. It is arising from the squamous occipital bone above the nuchal lines, and extends as far as, but not over, the parieto-occipital suture. (*Specimen No. 83A2, University College Hospital Museum.*)

which have been dealt with fully elsewhere. Sjoberg (1935) has described the osteomas of the maxillary antra, and Cushing (1927) and Armitage (1931) have described at length the tumours of the frontal sinuses, which are of special clinical importance, owing to their tendency to form intracranial mucoceles and aeroceles, and to give rise either spontaneously, or after attempted removal through the

sinuses, to cerebrospinal fistulæ and meningitis. Some of Cushing's tumours were said to arise from the ethmoidal bones, which, however, are cartilage bones. It is possible that these tumours were osteochondromas or that their origin was actually in the adjacent membrane bones.

A further group of osteomas of the skull which have been dealt with separately are the bilateral internal osteomas of the frontal bone. These tumours appear to be hormonic in origin, occur mainly in old people, especially females, and are associated with adiposity, virilism, and hyperplasia of the eosinophil cells of the pituitary gland, as described by Henschen (1937) under the title of the Morgagni syndrome.

The ivory osteomas are found in both sexes and tend to occur at a later age than the more fibrous forms. They are frequently preceded by a definite history of trauma and are slow-growing and painless, often coming to a standstill after

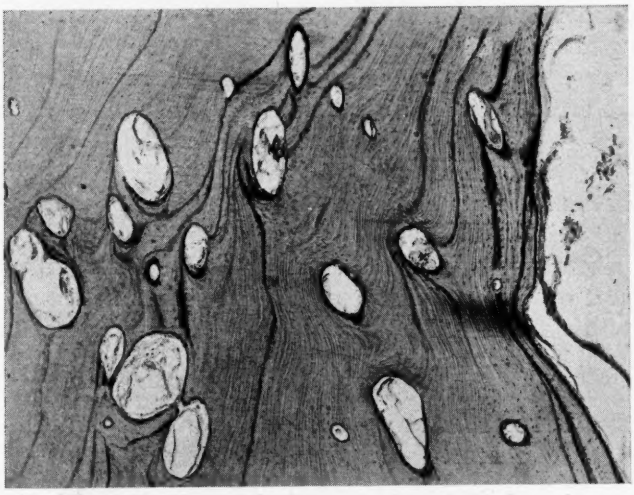

FIG. 247.—Low-power view of a section of a compact osteoma. The surface is covered by a thin layer of fibrous periosteum. The bone is mature, very dense and laminated with small haversian systems containing traces of bone-marrow. (H. and E.) (× 25.)

several years of growth. They are sometimes multiple, and Thoma (1934) has recorded a case in which there were several tumours on the vault of the skull, in the maxillary antrum, and on the mandible. On the vault of the skull they are usually symptomless, but in the external auditory meatus may give rise to deafness or otitis media, in the orbit to blindness by pressure on the optic nerves, and in the jaw may interfere with mastication or the fitting of dentures.

The usual form of sessile dome-shaped tumour lies like a limpet on the surface of the bone (*Fig.* 246). It is covered by a thin layer of periosteum, and the surface is very hard and frequently polished. Occasionally small compact pedunculated tumours are found, having a short stout pedicle and a mushroom-like head. They may be composed throughout of mature cortical bone, continuous with the outer table of the adjacent bone and formed of concentrically arranged laminæ containing small haversian systems and a little hæmopoietic or fibrous marrow (*Fig.* 247). In other forms there is a central core of cancellous bone with scanty fibrous tissue stroma, continuous with the medulla of the underlying bone. There is seldom

much evidence of remodelling, but the outer zone of compact bone is slowly enlarged at the expense of the underlying cancellous bone.

This represents the most mature and localized form of the fibro-osseous tumours of the membrane bones. It is periosteal or subperiosteal in origin, and although fibrous tissue may be almost absent, the tumour is formed in a similar manner to the more fibrous types, and all stages of transition are found between the two groups.

THE DIFFUSE OSTEOMAS

The diffuse osteomas of the skull and facial bones have in the past been grouped under the heading of leontiasis ossea. This was a term coined by Virchow to describe a group of cases with diffuse thickening of the skull and facial bones, analogous, he thought, to the thickening of the skin and subcutaneous tissues in leprosy, which had long been known as leontiasis. A great many cases have since been described under this title, which, however, is a purely descriptive one without any pathological basis.

Lawford Knaggs (1926) was the first to investigate these cases thoroughly, and after detailed examination of a large number of museum specimens he divided the available cases into two types—creeping periostitis and diffuse osteitis of the bones of the face and skull. The first group included the Peruvian skull and pugilist's skull in the Museum of the Royal College of Surgeons, and Bickersteth's case, and represented, he thought, a diffuse inflammatory periostitis originating in the vicinity of the accessory nasal sinuses and spreading from bone to bone, producing blockage of the nose and compression of the nerves in their foramina. The second group differed markedly from the first in its tendency to produce swelling of the whole bone and its conversion into a richly vascular porous new bone with the histological characters of osteitis fibrosa. He described the appearance of the surface of the bone as resembling a coarse woollen cloth, in which the salient contours were obscured and there was complete loss of differentiation between the cortical and cancellous layers. In this group he placed the Bristol and Jadelot skulls and described many other more circumscribed forms. The Bristol skull was from a patient with a generalized bone disease which closely resembles osteitis fibrosa cystica.

These diffuse osteomas, comprising Lawford Knagg's second group but excluding those cases of general bone disease, resemble the fibrous osteomas already described, but the disease instead of involving only one bone is affecting a number of adjacent bones. It shows the same tendency to arise early in life, though in a number of my cases the onset has been in middle age, to progress so far before becoming stationary, and frequently stops at a suture line. Each of the bones involved is swollen, its contours obscured, and the substances replaced by spongy new bone laid down in fibrous tissue and covered by a thin layer of cortical bone, perforated by numerous vascular foramina. The swelling is more pronounced in the direction of least resistance, i.e., into the mouth and on to the surface of the face and skull. The air sinuses are partially obliterated, but unlike the periosteal form nerve compression is unusual and the nose does not become blocked. The teeth are frequently carious, and once established the infection spreads rapidly and frequently persists in the diseased bone in the form of chronic sinuses and abscesses, possibly due to the decreased resistance to infection of the fibrosed marrow. The

facial contours are obliterated, and the surface of the bone is irregular and knobbly and the stretched skin telangiectatic. If the upper jaw is affected without the lower it projects out over it so that the teeth of the lower jaw fit inside those of the upper like a box within its lid. The upper jaw and frontal regions of the skull are most commonly involved, and I have seen five cases of this type. Horsley (1895) described five cases, four of which appear to have been examples of this or the more circumscribed type. Cases have also been described by Hale White (1896), Roberts (1896), Prince (1902), Bockenheimer (1908), and many others, but it is difficult to be certain of the exact nature of some of these early cases because of inadequate data.

FIG. 248.—Radiograph of an extensive osteoma involving the whole of the frontal region of the skull. The swelling is mainly on the outer side, and the edge is well defined and the substance mottled and spongy. The inner plate is depressed and wavy in outline.

An example of the disease in the frontal region of the skull is shown in *Fig.* 248. The radiograph shows an extensive osteoma which involved the whole of the frontal bone on each side, producing extensive deformity. The swelling is mainly on the outer aspect and is seen to consist of spongy new bone which has obliterated the outer table. The inner table is depressed and wavy in outline. The patient is a man of 62, and the disease dates from early childhood, but has produced no symptoms beyond deformity.

An example of the disease in the facial bones is afforded by the following case.

Case 6.—A man of 39 years complained of a swelling in the right cheek for six months. The lip was pushed forward by a bony tumour in the right maxillary region, most obvious from within the mouth, and extended just across the middle line. The teeth on that side were loose and carious and had recently been extracted. A radiograph showed an ill-defined mottled opacity in the right upper alveolar region, encroaching on the floor of the antrum; the remainder of the skeleton was normal. A biopsy was performed through the mouth and spongy bone removed, giving the typical appearance of osteitis fibrosa.

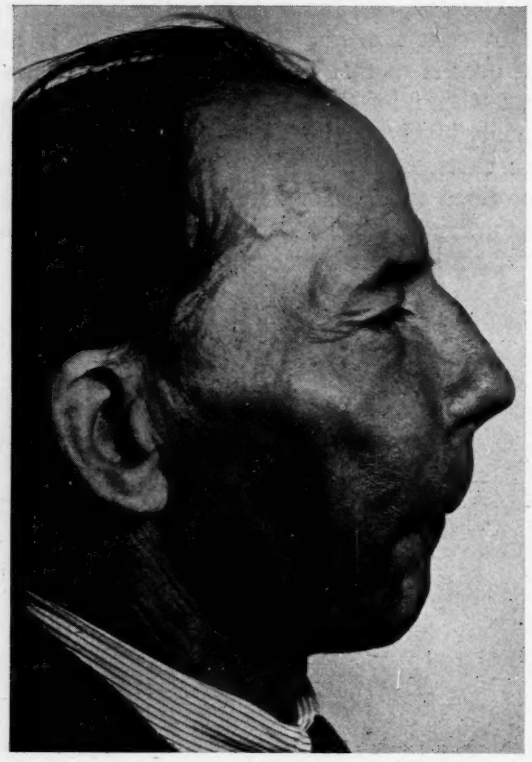

FIG. 249.—*Case* 6. Note the projection of the upper lip out over the lower lip and the filling up of the canine fossa and bulging of the cheek.

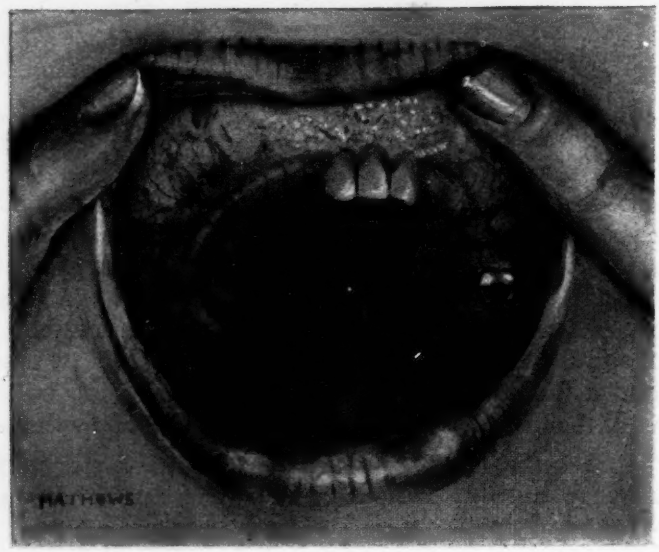

FIG. 250.—*Case* 6. The appearance of the hard palate, showing the generalized bony enlargement and slightly nodular surface. All the teeth except three incisors and one canine tooth have been extracted for caries.

The patient was discharged and was not seen again for ten years. He was then in excellent health and there was still no evidence of general disease. The swelling in the upper jaw, however, was considerably larger and jutted out over the lower lip (*Fig.* 249). The hard palate was entirely involved in the swelling, which consisted of smooth, soft new bone ; most of the teeth had been removed and the gums were healed (*Fig* 250). Both cheeks were rendered prominent by the swelling in the maxillæ, and the inferior orbital margins were slightly thickened. There was no epiphora, proptosis of the eyes, or nasal obstruction. A radiograph showed extensive disease of the whole of both maxillary bones, and replacement by dense new bone with a few rarefied areas within it (*Fig.* 251). Radiographs of the skull and remainder of the skeleton were normal ; the blood-calcium was 9·7 mg., and the phosphorus 3·9 mg.

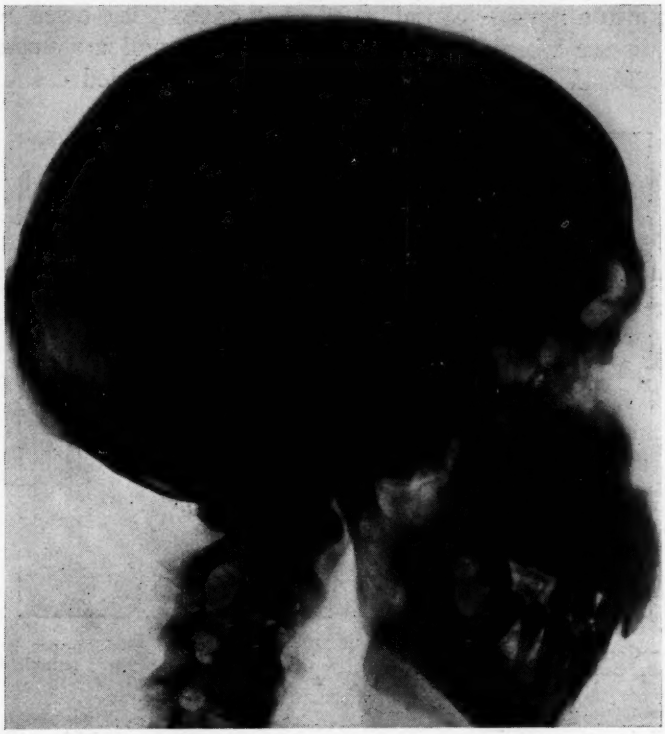

FIG. 251.—*Case* 6. Radiograph of the skull. The disease is limited to the upper jaw, which is converted into a mass of dense new bone with a few mottled areas of rarefaction.

The microscopic structure of the bone in these cases resembles that of the more localized fibrous osteomas. As a rule, practically the whole substance of the affected bones is involved with complete replacement of the marrow by fibrous tissue, in which the spongy new bone is laid down. One table of the bone may be partially preserved, and the outer surface of the tumour is covered by a thin layer of subperiosteal bone laid down parallel to the periosteum. The type and maturity of the bone within the substance of the tumour varies a good deal from case to case. Primitive woven bone, calcium spheroids, and laminated bone are found in a similar relationship to the fibrous stroma, as in the localized types. The trabeculæ pass in all directions, and may be slender, composed mostly of woven bone and separated widely by fibrous tissue, in the more spongy types ; and stouter, formed of laminated bone and separated only by narrow tracts of fibrous tissue,

in the denser types. Osteoclastic resorption of bone and re-formation of bone by osteoblasts may be active (*Fig.* 252), or the process may appear quiescent with evidence of extensive old remodelling.

In the past these cases have frequently been confused with the general skeletal diseases which are characterized by osteitis fibrosa. Cases of generalized osteitis fibrosa cystica are met with in which the skull and jaw bones are involved, and Hunter and Turnbull (1931) included one of these cases in their series. The bone is thickened, but osteoporosis causing mottling in the radiograph is the outstanding feature, and cystic areas and giant-celled tumours are frequently found, especially in the jaws.

There are also a number of published cases of leontiasis ossea associated with general bony disease which occur in young children and are unassociated with changes in the blood chemistry. In this group are included cases described by

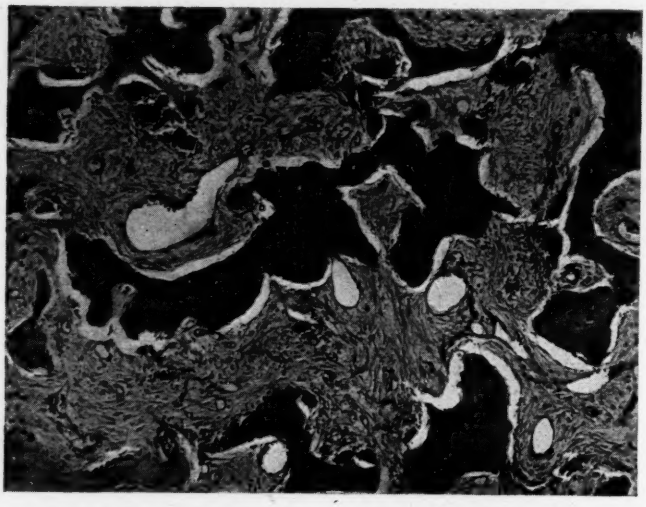

FIG. 252.—*Case* 6. Low-power view of a section of bone from the upper jaw. Note the mixed woven and laminated bone, the cellular fibrous stroma, and the active remodelling. (H. and E.) (× 65.)

Capon (1928), Ivimy (1929), Freedman (1933), and Gemmell (1935). Ivimy suggested that they were examples of juvenile Paget's disease, and Freedman supported this view, but Gemmell later maintained that they represented a clinical and roentgenological entity.

Paget (1877), when he described the disease of osteitis deformans, thought that the facial bones were never involved, and his belief has persisted in many quarters. Although it is rare, facial involvement does, however, occur, and then forms a prominent feature of the disease. There have been two examples in a series of thirty consecutive cases of osteitis deformans at University College Hospital, and Geschickter and Copeland (1936) found 3 in their series of 30 cases, so that it appears that the facial type represents about 8 or 9 per cent of all cases. The mandible may be affected as well as the remaining facial bones, and almost any combination of bones may be diseased.

Examples have been described by Prince (1902), Knaggs (1926), Seldin (1933), and others, and there is a skull in the Museum of University College Hospital

(*Fig.* 253) which shows this condition well. Severe caries of all the teeth was an outstanding feature in a case of this type which has recently been observed. The

FIG. 253.—A dried skull of a patient with the facial type of osteitis deformans. Note the extensive disease of the hard palate as well as the skull and the porous appearance of the bone. (*Specimen No.* 76A8, *University College Hospital Museum.*)

FIG. 254.—The interior of the mouth after the removal of all the carious teeth in a case of generalized osteitis deformans with facial involvement. Note the disease of both the upper and lower jaws. There is a chronic unhealed sinus in the right upper canine region.

patient, a man of 50 years, had complained of pains in the legs and deformity of the face for ten years. In addition to all the general characters of the disease, both cheeks were rendered prominent by thickening of the facial bones; both jaws were very swollen, and the teeth were loose and carious and there was an extensive periodontal bony infection (*Fig.* 254). Radiographs of the skull and jaws showed a mottled spongy appearance of the bones of the face with partial obliteration of the sinuses and the typical appearance of osteitis deformans in the skull (*Fig.* 255).

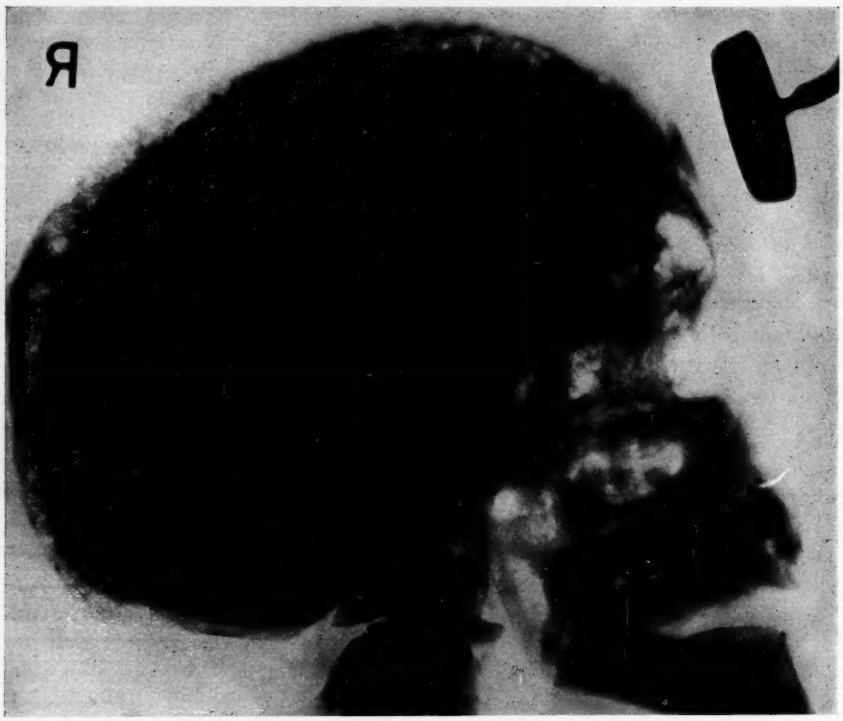

FIG. 255.—Radiograph of the skull in a case of osteitis deformans with facial involvement. Note the mottled sclerosis and rarefaction of all the facial bones.

The question, therefore, arises whether there is any relationship between the diffuse localized condition described and generalized osteitis deformans. Osteitis deformans is a disease which shows a tendency to involve certain bones and not others, and it is quite common to find cases infecting a single bone, such as the tibia or femur, for many years, without any evidence of a spread to the remainder of the skeleton, as described by Goldstein and Goldstein (1928). There is no reason why this should not occur in the facial and skull bones, and such cases have been described by Finkelstein (1932) and Thoma (1934). Lawford Knaggs (1926) thought that localized osteitis fibrosa and osteitis deformans were closely related diseases and represented the response to an unknown toxæmia, which in the young was adequate to confine the disease to a few bones, but in elderly patients was insufficient to prevent generalized disease.

The following case has presented some difficulty in diagnosis owing to its close resemblance to the facial type of Paget's disease, but without any spread to the remainder of the skeleton during four years' observation.

Case 7.—A man of 59 years complained of a painless enlargement of his face for fifteen years. There was no general disease but he had an irregular bony thickening of both upper jaws and frontal bones (*Fig.* 256). The lateral nasal furrows were filled up, the inferior orbital margins thickened, the zygomatic bones much enlarged, and the forehead unduly prominent. All the teeth in the upper jaw had recently been extracted owing to severe caries, and the gums shaved down, but the hard palate was obviously very much enlarged by soft spongy new bone formation. The left eye was displaced slightly upwards, but there was no diplopia. A radiograph showed that the disease was limited to the bones of the face and frontal region of the skull. The normal structure was obscured by spongy new bone formation, giving a cotton-wool appearance, the antrum and sinuses were practically obliterated, and the disease extended up as far as the coronal sutures. In the frontal bone there were numerous rounded sclerotic patches (*Fig.* 257). The blood Wassermann test was negative, the blood-calcium 9·7 mg., and phosphorus 4·4 mg. A course of treatment was given with the 1 gramme teleradiation unit, 32,000 mg. hours through four fields, but the disease remained stationary, and has not spread to the remainder of the skeleton while under observation for four years.

It would probably be possible to tell by microscopic examination of the bone in this case if it is an example of the diffuse osteomas of the membrane bones or a case of localized osteitis deformans, but unfortunately so far the opportunity has not been available.

Although the gross appearance of the bone in osteitis deformans and the spongy osteomas is very similar, there are certain microscopical differences. Fibrous tissue replacement of the fatty marrow is less extensive in Paget's disease and may be confined to the periphery of the bone trabeculæ. Woven fibrous bone and calcium spheroids are not frequent in the generalized disease, although I have found them to be present in the jaw bones in such cases. The regular interplay of resorption and re-formation of bone which gives rise to a mosaic appearance as described by Schmorl (1930) is the characteristic bony structure of osteitis deformans. It may also be found in places in the osteomas but is not typical.

AETIOLOGY

The group of benign fibro-osseous tumours under discussion have been shown to have a closely related pathological structure. They are characterized by the fibrous overgrowth of the periosteum or the replacement of the bone-marrow by fibrous tissue with erosion of the old bone and its replacement by new bone formed directly in the fibrous tissue by metaplasia. There is no hereditary or familial predisposition, and they are unassociated with general skeletal disease or a derangement of the calcium metabolism. This pathological condition which has been termed osteitis fibrosa is not restricted to these tumours, for it is found also at the site of healing fractures, in the walls of chronic hæmatomas and bone abscesses, and around new growths of bone (*Fig.* 258). It is the normal process by which injured bone anywhere in the body is repaired or diseased foci walled off. Geschickter and Copeland (1936) regard it as the normal healing reaction of bone, and a process of repair which forms a natural defence of the bone and periosteum against pathological invasion. They consider the giant-celled tumours of bone and localized osteitis fibrosa as opposite extremes of a single process, the former representing an excessive resorptive activity, and the latter a healing reaction. They

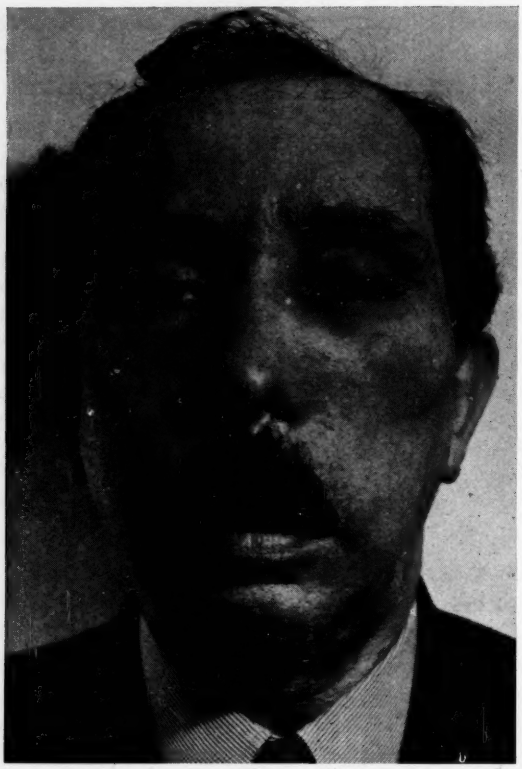

FIG. 256.—*Case* 7. Note the general obscuring of contours, the projection of the upper lip, and the slight upward displacement of the left eye.

FIG. 257.—*Case* 7. Radiograph of the skull showing the limitation of the disease to the facial and frontal regions and the similarity of the appearance to *Fig.* 255.

point out that both these conditions are commonly found, not only in the vicinity of diseased foci, but in relation to temporary structures in bone such as the epiphysial cartilages of the long bones and the deciduous teeth, where the processes of resorption and healing of bone are normally proceeding. They cite in evidence the occurrence of the giant-celled and fibrous epulis, in the region extending from the first molar on the one side to the first molar on the opposite side, in children and in young adults but not in infants, and they consider this as conclusive evidence of the relationship of these tumours to the deciduous teeth. In fact, however, these tumours are not entirely confined to the age period of 6 to 13 years, during which the deciduous teeth are shed, and I have one example of a fibro-osseous epulis which began at the age of 58, and another at 50 years. The association

FIG. 258.—Low-power view of section of bone from a hyperostosis of the mandible. A bony reaction of osteitis fibrosa has been produced around trabeculæ of secondary carcinoma. (H. and E.) (× 25.)

with infected teeth, on the other hand, is very striking, not only in the epulis, but in the central tumour of the jaw, and the relationship pathologically of the fibrous-osseous epulis to the central ossifying fibroma and the osteomas cannot be ignored.

In view of the frequent association of these tumours with chronic infection, it might be thought that they represent a chronic reaction of the bone to the irritation of carious teeth or infected sinuses. This view is supported by their natural tendency to grow slowly for some time, and later to become stationary when it might be assumed that the source of irritation has been overcome. There is, in fact, a type of chronic hypertrophic non-suppurative osteomyelitis of the jaws which closely simulates these tumours, of which there is an example, No. M2AF2, in University College Hospital Museum. In this case, which was before

the days of radiology, a large part of the lower jaw was resected in mistake for an osteoma, and it was only after splitting the specimen that a tiny central sequestrum was found. The bone was enormously swollen and spongy in appearance, and gave the microscopic appearance of osteitis fibrosa, with a few scattered inflammatory cells. Cases of chronic inflammatory obliterative sinusitis which resemble the fibrous osteomas have been described by Skillern (1936) and Collins (1939), and Wray (1915) and many others have commented on the association of chronic sinus infection with osteomas.

Infection, however, is inadequate to explain all these tumours, especially those skull osteomas unrelated to the sinuses. Moreover, carious teeth and infected sinuses are common conditions and might be incidental findings. In addition, it has been shown that in such conditions of general osteitis fibrosa as osteitis deformans there is a lowered resistance of the bone to infection which, in the facial type of the disease, results in the formation of chronic osteomyelitis round the roots of the teeth. It is possible that in all these conditions the infection is the result and not the cause of the osteitis fibrosa.

In a few cases, especially in the osteomas of the skull, there appears to be a striking relationship to injury which is a possible cause of a fibro-osseous overgrowth of the periosteum persisting for some time and then coming to rest. Injuries to the skull, however, are very common and notoriously difficult to evaluate aetiologically, and certainly trauma is not present in all cases.

Finally we are left with the possibility that these are true benign tumours related to the bones of the skull and face, in the same way as the osteochondromas are related to the growth of cartilage bones. This view is supported by the fact that they are found only in the membrane bones, sometimes arising from more than one focus, and start in the first half of life when growth is most active. Moreover, they are found most commonly in the frontal and facial regions, which are later to develop fully, and arise in the periosteal or subperiosteal regions which are the growing parts of the bones. They continue to grow slowly for many years, and, later, when growth in the skull is inactive, they become stationary. It is possible that such irritative factors as chronic infection or injury may initiate the process, but in the majority of cases they appear to arise spontaneously and without cause.

TREATMENT

The treatment of all these tumours is essentially conservative, and should be directed towards the prevention or cure of definite symptoms, rather than radical excision. The more fibrous tumours sometimes recur after incomplete removal, but there is no danger of malignant transformation, and a conservative operation can, if necessary, be repeated. The fibro-osseous epulis presents a simple problem, and should be removed together with the adjacent carious teeth, and, if necessary, a flake of the underlying alveolus. The central ossifying fibroma of the mandible can usually be excised, leaving enough bone to maintain the continuity of the jaw, but a bone-graft may be necessary to replace larger defects. In the maxilla the tumour can be scraped out through a Caldwell-Luc incision, but if it recurs and produces symptoms, as in *Case* 1, it may be worth while performing a limited resection of the upper jaw and fitting an obturator.

In the absence of pressure symptoms the localized osteomas should be left alone, or only enough of the tumour removed to give a satisfactory cosmetic result. The compact osteomas are so hard that it is often extremely difficult to cut through them. The osteomas of the frontal sinuses and the orbits, owing to their serious complications, require to be tackled early. As Cushing (1927) has shown, it is better to approach the deep-seated sinus osteomas intracranially by stripping back the dura after raising a frontal osteoplastic flap than to approach them through the sinuses and risk a cerebrospinal fistula. Small orbital osteomas may be approached directly through the orbit, but when they are extensive and compress the optic nerve further back, the intracranial approach is preferable. It is frequently only possible to cut away enough of the tumour to free the nerve.

In the localized and diffuse forms of fibrous osteomas, carious teeth must be eradicated and care taken to avoid the setting up of chronic osteomyelitis. The infected sinuses require to be drained and the linings removed. Osteomas projecting intracranially and giving rise to epileptic fits can be raised within an osteoplastic flap. The projecting part of the tumour should then be shaved off and the remainder of the flap replaced. In the more extensive cases it is not possible to do anything except deal with septic foci. It is possible that X-ray irradiation may relieve pain if it should be present, but there is no evidence that it controls the course of the disease.

SUMMARY

1. There is a group of benign fibro-osseous tumours of the membrane bones of the vault of the skull and face which are unassociated with general skeletal disease, and though differing in their clinical characters and pathological details have an essentially similar structure. They arise in one or more foci, usually early in life, and grow slowly for many years before becoming stationary. All stages of bone formation in fibrous tissue are found within these tumours, and frequently an abortive form of ossification resulting in the formation of calcium spheroids.

2. Four main varieties have been described: the ossifying fibromas, the fibrous osteomas, the compact osteomas, and the diffuse osteomas. They arise periosteally or subperiosteally, and remain localized or involve the whole of one or several adjacent bones.

2. Some of the localized tumours are associated with chronic infection or injury, and it is possible that they represent a form of fibro-osseous reaction of the bone and periosteum to the chronic irritation of sepsis or to trauma, both of which are known to be capable of producing such a reaction in bone.

4. The majority of the tumours, however, cannot be attributed to any form of irritation. Their limitation to the membrane bones, often in multiple foci, and their origin frequently during the growth period, suggests that they are true benign tumours related to the development of the membrane bones and comparable with the osteochondromas of the cartilage bones.

5. Their treatment should be conservative and limited to the relief of symptoms.

I am indebted to the staff of University College Hospital and to Mr. Stanford Cade, Mr. E. D. Davis, and Mr. Harvey Jackson for their kind permission to use their cases, and to Professor H. Turnbull and to Professor A. Amies for their help in this pathological study.

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THE PATHOLOGY, DIAGNOSIS, AND TREATMENT OF HASHIMOTO'S DISEASE (STRUMA LYMPHOMATOSA)

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HISTORICAL SUMMARY

Riedel, in 1896, 1897, and again in 1910, described a form of goitre which he referred to as 'eisenharte' because of its peculiar consistency. In the limited series of cases which he observed young adults were affected, males more often than

females, and the essential clinical feature was the widespread involvement of the extrathyroid tissues in a diffuse sclerosis which appeared to have originated in part of the thyroid gland—a state of affairs which precluded radical surgical excision owing to the danger of damage to the trachea, œsophagus, great vessels, and nerves. Riedel stressed the absence of evidence of functional disorder of the gland, whether before or after operation, and he made no mention of any lymphoid infiltration in his histological description of the tissue removed surgically.

In 1912 Hashimoto reported 4 cases of a peculiar type of 'lymphoid goitre', by which term, he says, "I understand a growth of the lymphatic elements and a formation of lymphoid follicles together with certain changes both in the parenchyma and in the interstitial tissue of the excised gland". He expressly states that the lesion had not been recognized previously, and that he regarded it as distinct from Riedel's disease as well as from chronic thyroiditis, specific and non-specific. In 1925, and in greater detail in 1929, Williamson and Pearse described the same condition under the name 'lymphadenoid goitre', to which the objection is cogent that eponymically Hashimoto's term 'struma lymphomatosa' is undoubtedly correct, while in addition there is a faint suggestion implied in the word 'lymphadenoid' of an association with lymphadenoma, to which in fact it has no real resemblance.

Between 1912 and 1922 scant attention appears to have been paid to Hashimoto's work, and, except for Heineke's article in 1914, little or nothing bearing on the subject was published until in 1922 Ewing, basing his opinion on the study of four cases only, came to the conclusion that Hashimoto and Riedel had described the earlier and later stages respectively of the same disease, which he designated *benign granuloma of the thyroid*, a name previously used by Meyer (1913) for Riedel's disease itself. Ewing stated that in the four cases he studied, the gland was *bilaterally involved*, and that in one of them a *large goitre was present which receded after radium therapy*.

Ewing's views were apparently widely accepted, with the result that all attempt to differentiate between the two conditions ceased, and as a consequence nearly all cases germane since 1922 have appeared under one or other of the many synonymous titles for Riedel's disease such as :—

1. Fibroid enlargement of the thyroid (Semple, 1868–69).
2. Infiltrating fibroid tumour of the thyroid (Bowlby, 1885).
3. Eisenharte Tumoren der Schilddrüse (Riedel, 1896).
4. Inflammation chronique primitive cancériforme de la glande thyroïde (Tailhefer, 1898).
5. Primary chronic inflammation of the thyroid (Berry, 1901).
6. La dégénération fibreuse du corps thyroïde (Poncet, Ricard, 1901).
7. Riedel'sche Struma (Spannaus, 1910).
8. La thyroïdite ligneuse cancériforme (Alamartine, 1911).
9. La thyroïdite ligneuse (Delore and Amartine, 1911).
10. Ligneous thyroiditis (Murray and Southam, 1912).
11. Thyroiditis chronica maligna (Meyer, 1913).
12. Die chronische Thyreoiditis (Heineke, 1914).
13. Benign granuloma (Ewing, 1922 ; Heyd, 1929).
14. Thyroïdite ligneuse chronique (Monod and Monod, 1923).
15. Chronic productive thyroiditis (St. George, 1924).
16. Non-suppurative chronic thyroiditis (Hahn, 1925).
17. Riedel's struma (Meeker, 1925).
18. Riedel's chronic thyroiditis (Shaw and Smith, 1925).
19. Chronic ligneous thyroiditis (Smith and Clute, 1926).
20. Thyroiditis simplex (Riedel's tumour) (Bruce, 1931).

To mention one example of the confusion which has resulted I cannot do better than refer to Shaw and Smith's article which appeared in 1925 under the title of "Six Cases of Riedel's Thyroiditis" Graham (1931), after a careful analysis of these cases, is not satisfied that any one of them conforms to Riedel's description, an opinion with which I am in complete agreement, confirmed as it is by an examination of the pathological material from those cases.

If, then, as I hope to be able to show, Ewing's generalization is erroneous in that at least two different entities have been merged in this welter of titles, it seems hardly premature to attempt to define what in fact constitutes Hashimoto's struma: secondly, to contrast it with Riedel's disease, not ignoring the fact that the latter name has been applied very loosely, especially since 1912, and to a diversity of conditions more or less remote from what Riedel did in fact describe. Thus Eason (1927–8) makes the astonishing statement (for which I can find no published reference) that "some pathologists insist that Riedel's struma should not be diagnosed *unless they have satisfied themselves that the so-called germinal centres are present*". He also states that Riedel's disease normally begins diffusely, although both Riedel and Hashimoto expressly deny this. Even more recently Renton, Charteris, and Heggie (1938) assert that Riedel's disease is characterized by lymphocytic infiltration with or without giant cells, a view which explains why all their cases conform very closely indeed to Hashimoto's description but differ markedly from Riedel's.

It must not be concluded, however, that no attempt has yet been made to establish the soundness of Hashimoto's views, for Heineke (1914) certainly differentiated between the two groups of cases, and Reist (1922) could not agree that they were quite one and the same disease. Furthermore Perman and Wahlgren (1927), in reporting a case of true Riedel's disease, were able to show that the pathological tissue removed at two operations separated by a year's interval was of almost identical histological structure, thus combating the view that in the earlier stages of Riedel's disease the histological features correspond to what Hashimoto described. Graham and McCullagh (1931), and again a little later Graham (1931), first focused attention on the accumulated evidence that Riedel's disease and struma lymphomatosa are distinct and distinguishable diseases. Graham (1931) also pointed out the polygenous nature of the 104 cases which he reviewed from the literature, and was able to differentiate them into ten groups, only 41 of the cases being acceptable as Riedel's disease and 24 as struma lymphomatosa, the remaining 39 being attributed to various forms of chronic thyroiditis, atrophy and fibrosis, hyperthyroidism, etc. In my own *Diseases of the Thyroid Gland*, which though published in 1932 had gone to press before I had the advantage of studying Graham's papers, I briefly summed up the evidence in favour of the view that 'lymphadenoid' goitre is distinct from Riedel's disease, but unfortunately I had not read Hashimoto's original communication and was unaware that that term, introduced by Williamson and Pearse (1925), must cede precedence to 'struma lymphomatosa' given to it by Hashimoto thirteen years previously.

Following on Graham's admirable analysis, other authors have described cases of Hashimoto's struma clearly differentiated from the Riedel conglomeration: among these are Howard (1934), Clute, Eckerson, and Warren (1935), Emerson (1935), Mallory (1935), Poer, Davison, and Bishop (1936), and McClintock and Wright (1937), though Polowe (1934) appears to have confused the lymphoid type of thyrotoxic goitre with struma lymphomatosa.

Many other recent writers have labelled cases which conform closely to Hashimoto's description under the term Riedel's disease or its cognomina, notably Renton, Charteris, and Heggie (1938), who in their otherwise exemplary report on the treatment of Riedel's thyroiditis by radium are certainly referring to Hashimoto's struma. Kreuzbauer (1930 and 1931) maintains, on the other hand, that there is no need to differentiate the two types of goitre, for he says some of them have lymph follicles and others not, and Jaffé (1937) also supports Ewing by urging that the differences between Hashimoto's struma and Riedel's disease are qualitative only, yet he finds justification for separating them on clinical grounds. Much of Jaffé's material was obtained at autopsy from the subjects of advanced systemic disease, and in none did the thyroid weigh more than 25 g., so that these cases, unlike Hashimoto's, cannot be regarded as goitrous, and his conclusions are therefore applicable more strictly to the atrophic forms of lymphoid infiltration of the thyroid met with particularly in elderly hypothyroid subjects.

De Quervain (1904, 1906), and De Quervain and Giordanengo (1936), have done much to clarify the situation, though approaching it from another aspect. In their comprehensive review of the whole subject of non-suppurative thyroiditis and strumitis they demonstrate the stages which lead from acute through subacute on to chronic thyroiditis, leaving open the question as to whether Riedel's disease is merely an advanced form of the last-named or a specific lesion of the gland. They also amplify and modify the conclusions reached by Roger and Garnier (1900), Farrant (1913–14), Clute and Smith (1927), Burhans (1928), Cole and Womack (1928, 1929), Bérard and Dunet (1929), and Leffmann (1932) as to the pathological effects of various toxic and infectious diseases on the thyroid gland. None of these authorities describes anything comparable to what is seen in struma lymphomatosa in any stage of development, a fact which argues strongly against its toxic or inflammatory origin, and de Quervain and Giordanengo add that they could find nothing to indicate that Hashimoto's struma is directly related to any of the forms of acute, sub-acute, or chronic thyroiditis or strumitis studied by them in their very complete survey, which includes both specific (i.e., tuberculous, syphilitic, actinomycotic, etc.) and non-specific forms. They conclude that it is a distinct disease "found particularly in England and Japan", a statement of distribution which, as will appear later, is far too narrowly defined.

INCIDENCE

It is difficult for reasons which are indicated in the earlier part of this paper to assess the frequency of Hashimoto's struma, and Graham in 1931 was able to identify only 24 cases in the literature, a figure increased to 50 by McClintock and Wright in 1937, since when there have been few cases recorded. Inquiries made by me among surgeons in Great Britain who have had special experience in thyroid surgery lead me to suppose that the condition is not nearly so rare as the figures quoted would imply. In addition, an examination of the material from pathological museums in London, Edinburgh, and the provinces, reveals a considerable number of specimens of struma lymphomatosa, and incidentally very few of true Riedel's disease. In the aggregate I am able to add a total of 81 cases, 51 from my own practice, and 30 (hitherto unpublished) communicated to me. The relative frequency among thyroid diseases generally is shown as follows :—

	Hashimoto's Struma	*Riedel's Disease*	*Total Thyroidectomies*
J. Graham* (Edinburgh)	6 cases (0·9 per cent)	2 cases (0·3 per cent)	670
Renton, Charteris, and Heggie (Glasgow, 1938)	7 cases (1·7 per cent)	—	418
G. Keynes*	25 cases	—	1600
C. A. Joll	51 cases (0·9 per cent)	10 cases (0·18 per cent)	5650 (up to January, 1939)

(It is worthy of note that from the same material only 5 unpublished examples of indubitable Riedel's disease were identified, compared with 81 of Hashimoto's struma.)

Age Incidence.—Hashimoto's disease is rare before 40, but may occur into the eighth decade—thus Graham's oldest patient was 75 and one of mine 74. I have, however, a note of a case in a girl aged 10, and a few are on record between 20 and 40. In Riedel's disease, speaking generally, the incidence is certainly earlier, whereas on the basis of Ewing's views the reverse should be the case (*Fig.* 529).

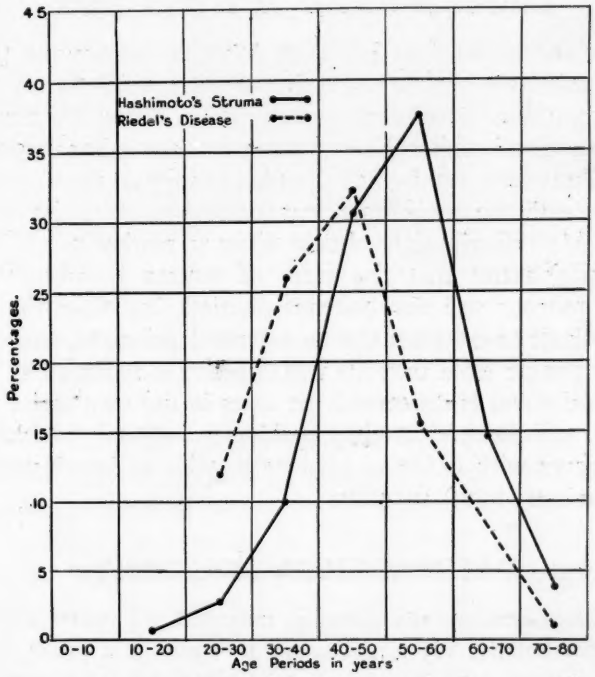

FIG. 259.—Age incidence of 106 cases of Hashimoto's struma compared with 89 cases of Riedel's disease. (Author's collected series added to Lee's figures.)

It must not be forgotten that Eisen (1934) takes a diametrically opposed view and believes that Riedel's disease is the earlier and Hashimoto's struma the later stage of one disease, though the evidence for this view seems too slender to require refutation.

Sex Incidence.—There is a striking preponderance of women among the cases of struma lymphomatosa, both in McClintock and Wright's and in my own

* Personal communications.

series, the discrepancy between the two groups being negligible, whereas in Riedel's disease, although the later figures do not bear out the original contention that the disease is commoner in males, the disproportion between the sexes is much less than for the former disease, and probably bears some relationship to the sex incidence of thyroid disease generally in any particular district. The sex distinction between the two conditions is sufficient at once to indicate that they cannot be mere stages in one disease, unless it be assumed that in an inordinate number of females suffering from Hashimoto's struma there is spontaneous recovery, and that conversely in an overwhelming number of males similarly affected the lesion passes into Riedel's disease. Even if the latter possibility were assumed, the relative frequency of the two conditions, so far as they are revealed by the available statistics, precludes such a transference, for the total number of cases of struma lymphomatosa (obtained by adding McClintock and Wright's and the author's series) is 131, while the corresponding figure for Riedel's disease is 65. On such figures, therefore, it is impossible to account for the number of cases of Riedel's disease recorded among males on the basis of a transformation from struma lymphomatosa.

GEOGRAPHICAL DISTRIBUTION

De Quervain, of Berne, and Haas, of Munich, inform me that Hashimoto's struma is almost unknown in their respective districts, yet it occurs elsewhere on the continent of Europe, but is certainly commoner in Great Britain and possibly in America and Japan than is either Riedel's disease or any other non-suppurative form of thyroiditis. These facts, few as they are, tend to support the view that Hashimoto's struma and Riedel's disease are independent conditions, otherwise it seems incredible that their geographical distributions should differ so markedly.

Emerson (1935) states that the cases of struma lymphomatosa are equally divided between goitrous and non-goitrous districts, but from the figures available it would seem difficult to establish this as a general principle, and of my own series of 51 cases, only 5 came from districts where goitre is regarded as endemic.

So far as *social status* is concerned the cases in my own series were distributed among all classes, and there is certainly nothing to indicate that the disease has any connexion whatsoever with defective hygiene or with an insufficient or ill-balanced dietary as McCarrison (1929) suggests.

PATHOLOGICAL ANATOMY

In struma lymphomatosa the gland is enlarged, all parts of it sharing in this enlargement proportionally. It is necessary to stress this point, since it has been alleged that one or other lobe may be affected either preponderantly or exclusively. It must be remembered that the normal thyroid may be asymmetrical, sometimes so much so that one lobe may be entirely absent; consequently if Hashimoto's struma affects such a lopsided gland, the asymmetry will be exaggerated. In none of the cases in my own series was the lesion other than generalized, a feature which at once distinguishes it from the focal lymphoid infiltration so common in certain types of thyrotoxic goitre. The pyramidal lobe, as well as substernal prolongations when present, also shares in the general enlargement, and very commonly indeed there is a striking degree of enlargement posteriorly, so that the lobes meet or even overlap behind the pharynx, larynx, and œsophagus ('circular goitre'), resulting

in antero-posterior compression of the trachea, though this is rarely sufficient to cause serious dyspnœa (*Fig.* 261).

The surface of the gland is smooth and slightly lobulated, this lobulation being merely an exaggeration of the normal (*Fig.* 260). The superficial veins are not as

FIG. 260.—Hashimoto's struma. From a woman aged 48. Note widespread involvement, including pyramidal lobe, absence of adherent muscle tissue, and exaggeration of the pseudo-lobular appearance due to increased fibrosis. (*Natural size.*)

large as in many thyrotoxic and nodular goitres of comparable size and the capsule of the gland, though slightly thickened, is smooth externally and shows no evidence of adherent muscular or fascial tissue. After removal the solidity of the tissue is revealed by the depth of the groove in which lay the trachea, which may consequently be bilaterally compressed in the larger and more fibrous goitres. There is often some thickening of the capsule where it lies in contact with the trachea, but nothing to indicate any direct fibrous infiltration of the tracheal wall from the goitre or vice versa. One of the main anatomical supports of the thyroid, possibly the most important, is the fascial attachment between the gland and the tracheal wall, and it is this fascial tissue which becomes hypertrophied in all large and heavy goitres, but however great this hypertrophy it bears no sort of resemblance to the solid block of dense fibrous tissue which engulfs the trachea in Riedel's disease.

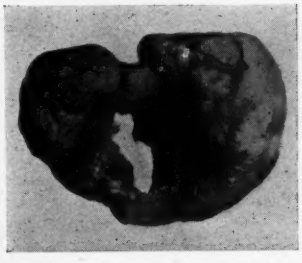

FIG. 261.—'Circular' form of goitre common in Hashimoto's struma.

In struma lymphomatosa the consistency of the gland tissue is quite uniform throughout, best revealed when complete thyroidectomy has been performed in the

erroneous belief that the condition is neoplastic. There is a wide difference between the relative friability of the early stage and the resilient toughness of the later stage, though this latter is never sufficient to justify the terms 'iron-hard' or 'woody' which are so apt for Riedel's disease. On section in the earlier stages the tissue

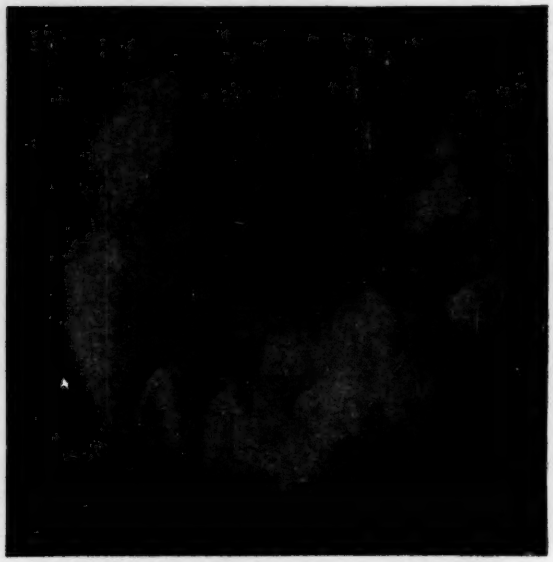

FIG. 262.—Hashimoto's struma. From a woman aged 58. The uniform pink colour and the complete symmetry are well shown.

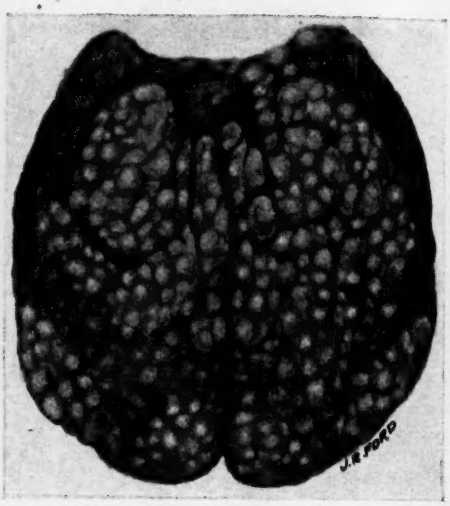

FIG. 263.—Hashimoto's struma. From a woman aged 50. The whole gland is uniformly affected, but there is no extra-thyroid extension.

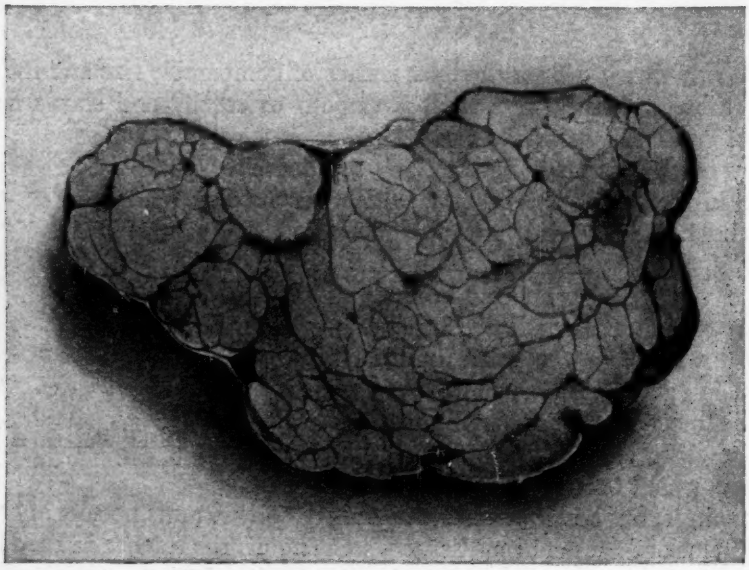

FIG. 264.—Hashimoto's struma. From a woman aged 55. The stroma is abnormally developed, resulting in a pseudo-lobulation.

may be as friable as that of a lymph-node, and it is only in the advanced stages that it can be said to grate on the knife, little, if any, juice being then expressible.

The colour of the gland tissue varies from the palest pink (*Fig.* 262) to yellowish white (*Fig.* 263), with a distinct brownish tinge in certain specimens. In fresh material in early stages of the disease there is often a suggestion of translucency.

The capsule shows slight to moderate thickening and the connective-tissue stroma is abnormally distinct even in the earlier stage, though later it stands out very clearly as thick fibrous bands (*Fig.* 264): in the most advanced degree of fibrosis the pseudolobular structure may be obscured rather than emphasized.

The main blood-vessels are not as large as in either simple or thyrotoxic goitres of comparable size and the general vascularity is diminished. The blood-vessels show no special tendency to be thickened or otherwise abnormal.

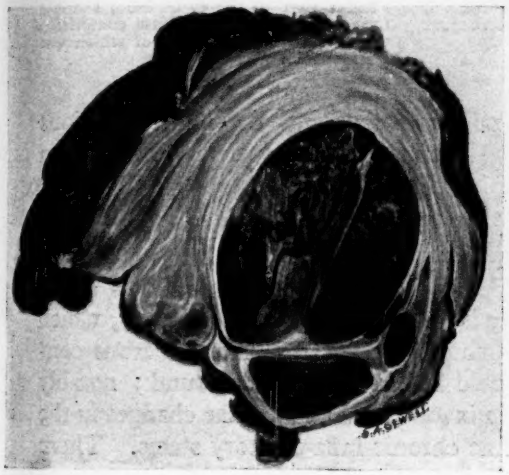

FIG. 265.—Riedel's disease affecting colloid goitre. From a woman aged 38. Note the adherent muscle and the opaque fibrous tissue surrounding colloid goitrous nodule.

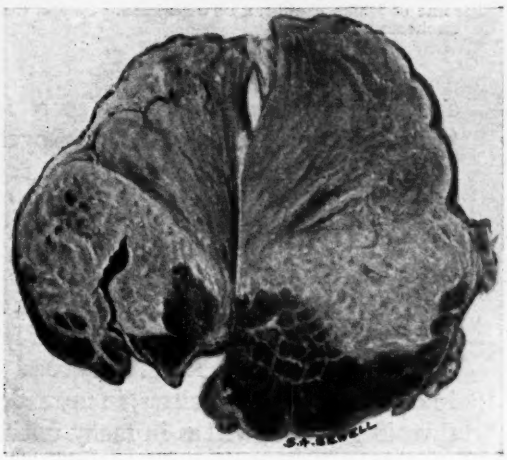

FIG. 266.—Riedel's disease. From a woman aged 29. Note the distribution of the fibrosis and the zone of relatively unaffected thyroid tissue below.

There is no naked-eye evidence of normal colloid-containing tissue to be seen in any part of the gland and nodules and cysts are very rare, and doubtless when present their formation antedated the lymphoid change. Neither necrosis, calcification, nor abscess formation has been observed in any specimen examined by me.

Comparison with Riedel's Disease and Allied Disorders.—Contrast with the above description the state of affairs in *Riedel's disease*, in which the pathological changes are usually unilateral, at any rate in the earlier stages: the mass is seldom as large as a goose's egg, and the shape of the gland is obscured by adherent fragments of muscle tissue, etc., while its hardness on section is sufficient to blunt the knife. The cut surface is a dull white or yellowish white (*Figs.* 267, 268), there is no trace of 'pseudo-lobulation', yet at some point or points areas of colloid-containing tissue may be clearly visible and even occasionally a cyst or small areas of calcification (*Figs.* 265, 266). In *syphilitic chronic thyroiditis* there is usually gross evidence of necrosis of a gummatous type which is characteristic,

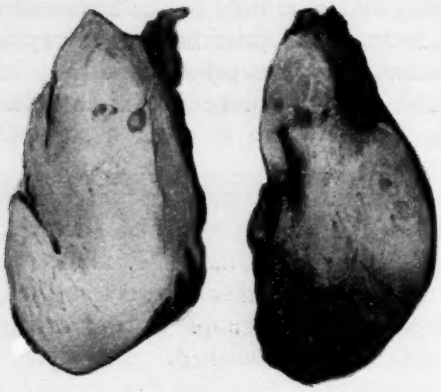

FIG. 267.—Riedel's disease. From a woman aged 34, with extreme dyspnœa and evidence of tracheal compression. The two fragments shown represent only portions of the pathological material, some of which could not be extirpated. Patient wears a permanent tracheotomy tube.

FIG. 268.—Riedel's disease. From a woman aged 38. The mass represents the greater part of the right lobe, but not the whole of the fibrous mass comprising the original swelling, part of which was irremovable.

and in *tuberculous thyroiditis* (apart from miliary forms and the highly dubious 'tuberculose inflammatoire' of Roger and Garnier) caseous foci are to be seen both in the gland tissue and in the regional lymph-nodes.

MORBID HISTOLOGY

Microscopically the characteristic feature is the *uniformity of the changes*, which at once serves to distinguish struma lymphomatosa proper from the numerous conditions in which some degree of focal lymphoid infiltration may be found; notably in certain thyrotoxic goitres, in myxœdema, in involutional and similar changes in the thyroid gland, as well as in many unclassifiable chronic inflammatory states. There

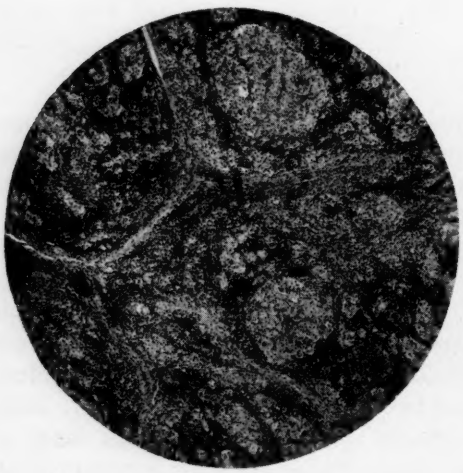

FIG. 269.—Hashimoto's struma. Photomicrograph showing diffuse infiltration with leucocytes and widespread changes in the parenchyma. (× 27.)

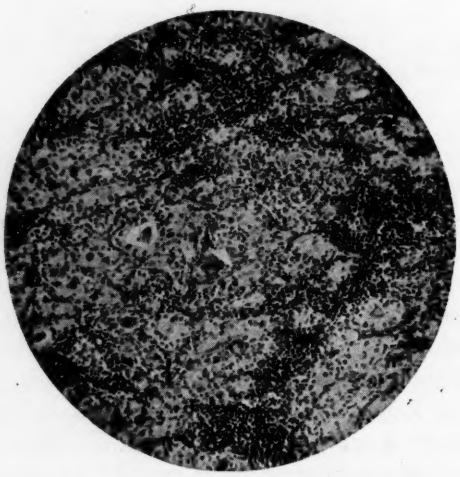

FIG. 270.—Photomicrograph from same specimen as in *Fig.* 269 under higher power. (× 74.)

is a *diffuse* lymphocytic infiltration as well as more or less numerous *focal aggregations*, some with, some without, *germinal centres* (*Figs.* 269, 270). These changes are widespread, so that in all parts of the gland the appearances under the microscope are very similar. This does not preclude considerable differences in detail according to the stage reached by the disease, as Hashimoto himself admits, and it is these that have led Ewing and others astray and into assuming that in the final fibrotic stage there is a pathological identity with Riedel's disease. My able colleague, Vaux (1938), working largely with recent material from my clinic, has differentiated three stages—early, intermediate, and late—correlating these in a general way with the clinical features. In her opinion there is a definite gradation in the degree of parenchymatous destruction and the amount of fibrosis, the average age of patients corresponding with what would be expected in the three gradations (*Fig.* 271). Vaux also maintains that in the early stage there is evidence of thyrotoxicosis in a

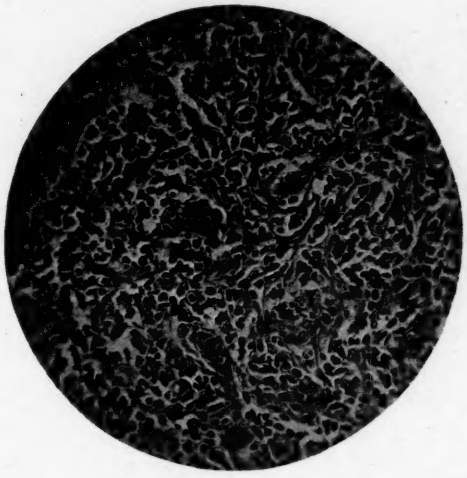

FIG. 271.—Hashimoto's struma. Photomicrograph from an advanced case (*see Fig.* 298) with fibrosis and total disappearance of vesicular tissue. (× 150.)

majority of cases, this, however, diminishing in the intermediate stage, passing eventually into hypothyroidism in the last stage. Several of the cases included by Vaux as being in the earlier stages would not, in my opinion, be justifiably included under Hashimoto's struma, but should be classed with the advanced forms of lymphoid infiltration in Graves' disease, and therefore the validity of her conclusions must be judged accordingly. McClintock and Wright (1937) report a case in a woman of 53 on whom two operations were done at an interval of two years, the extirpated tissue at both stages having essentially the same structure with a little added fibrosis in that removed later. I have had a similar case (*R.C.H.* series No. 1), the interval between the operations being more than four years, and although Heyd (1929) claimed to have observed a definite transformation of struma lymphomatosa into Riedel's disease from material similarly removed at intervals from the same patient, McClintock and Wright maintain that the extirpated tissue in both stages has the structure of Hashimoto's struma.

1. **The Lymphatic Elements.**—A diffuse lymphocytic infiltration is constantly present and involves widely the intervesicular connective tissue (*Fig.* 273).

*The lymph-follicles** vary greatly in size and number; they are usually rounded, but may be polygonal, fusiform, or irregular in shape. As a rule they possess a germ centre demarcated from the surrounding tissue by several layers of lymphocytes

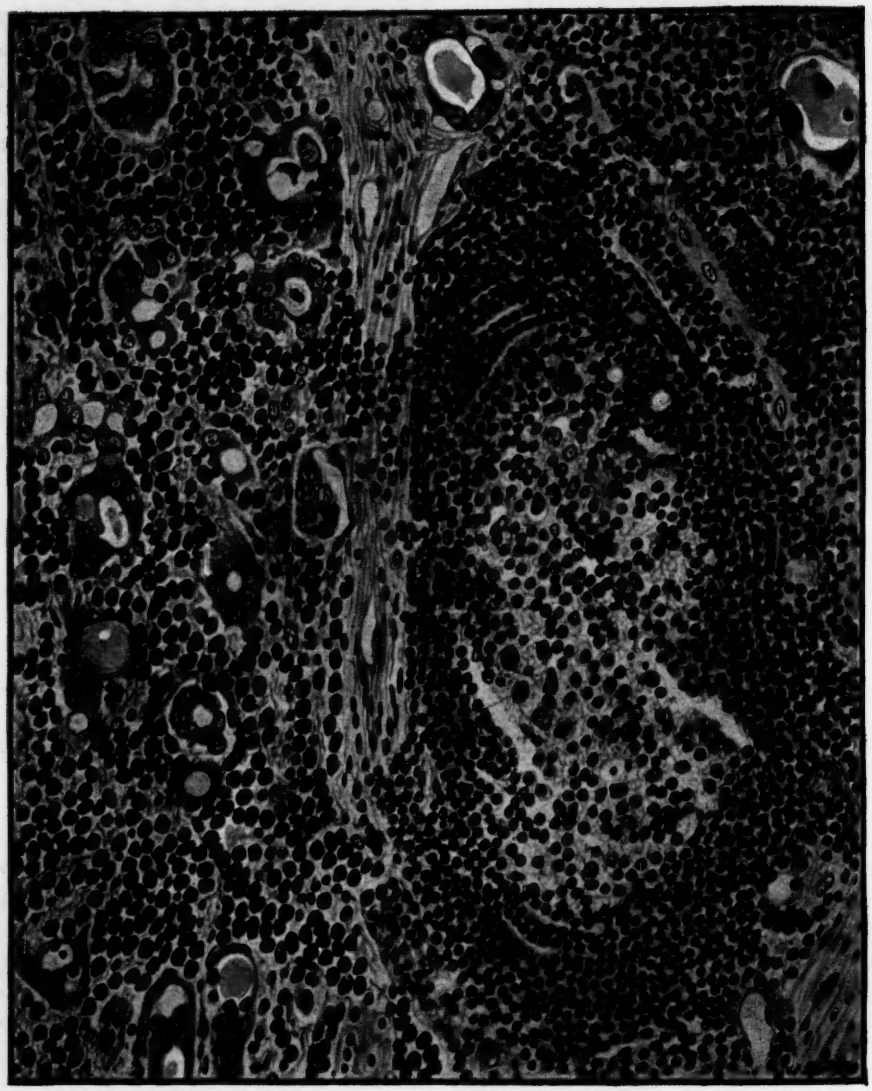

FIG. 272.—Hashimoto's struma, showing structure of a large lymphoid follicle with germinal centre. There is some increase in the fibrous stroma and several degenerate vesicles, a few with traces of colloid. (× 300.)

arranged fairly regularly in rows. In the germ centres are: (*a*) Reticulum cells, with large pale vesicular nuclei, some showing mitosis; (*b*) Plasma cells in small

* In this article, in order to avoid confusion, as far as possible the term *follicle* is restricted to the lymphocytic structures, while the term *vesicle* is employed for the epithelial thyroid unit.

numbers, with eccentrically placed nuclei and a characteristic chromatin network; (*c*) Scattered lymphocytes (*Fig.* 272).

These lymph-follicles must not be confused with the pseudo-follicles which are common in many types of goitrous glands and in myxœdema. These have a superficial resemblance to true follicles, but do not exhibit the germ-centre structure as described above, the central areas containing sometimes rather large pale cell remnants of thyroid epithelium or in others collections of phagocytic leucocytes. Both true and pseudo-follicles may be found in certain examples of struma lymphomatosa.

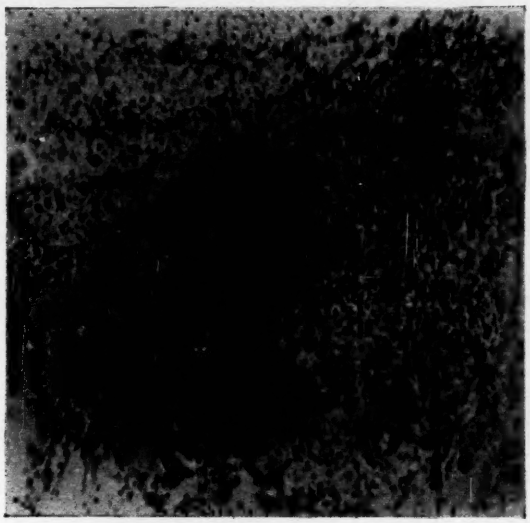

FIG. 273.—Hashimoto's struma. From a woman aged 50. Diffuse lymphocytosis, fragments of colloid, and widespread changes in the epithelium coexist with little fibrosis. From a photomicrograph in colour. (× 120.)

2. The Thyroid Vesicles.—These also show great differences in size (Hashimoto's measurements were 30 to 360μ), but in my material large vesicles are rare, the majority being of the order of 70μ (*Fig.* 274). In shape they may be oval, rounded, or irregular, or all trace of vesicular structure may be lost, a syncytium resulting. The interstitial connective tissue is hyperplastic and may contain epithelial cells either scattered or in groups. In one of my cases the vesicles show an extraordinary variety of metaplasia to squamous-celled tissue with well-marked keratinization, and a somewhat similar appearance is described by Kreuzbauer (1931).

The *cells* lining the vesicles are flat to low-columnar, according to the amount of colloid which persists. They are usually in a single layer, their protoplasm staining very variably with eosin. The nucleus is basal in the taller cells and central in the flatter; it is oval or rounded, with from one to four nucleoli. In the later stages the epithelial cells of the atrophic vesicles are large, acidophil, with excessive granular protoplasm and hyperchromatic nuclei. Occasionally the epithelial cells, both isolated and in vesicular formation, contain granules staining black with Flemming's solution or reddish with Sudan III or Scharlach R. These may, as

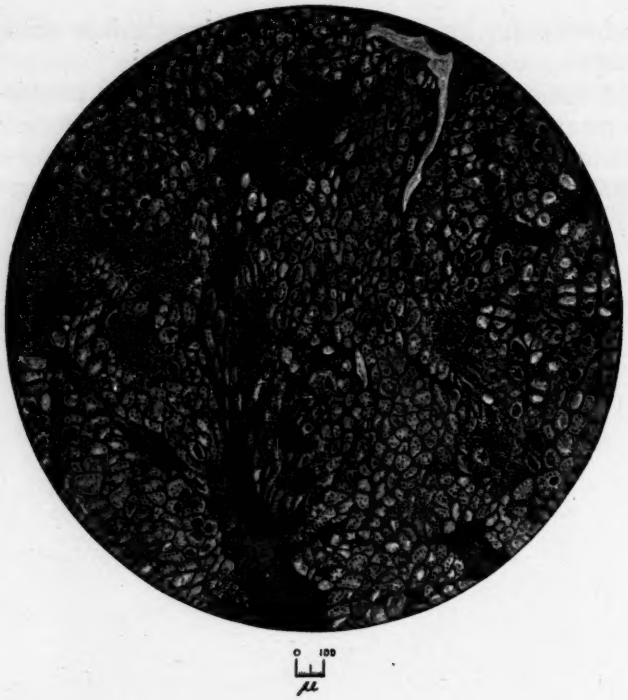

FIG. 274.—Hashimoto's struma. Drawing from a section stained by Gallego's method. The diffuse fibrosis (blue), lymphocytic infiltration (purple), and parenchymatous degeneration are shown. (× 35.)

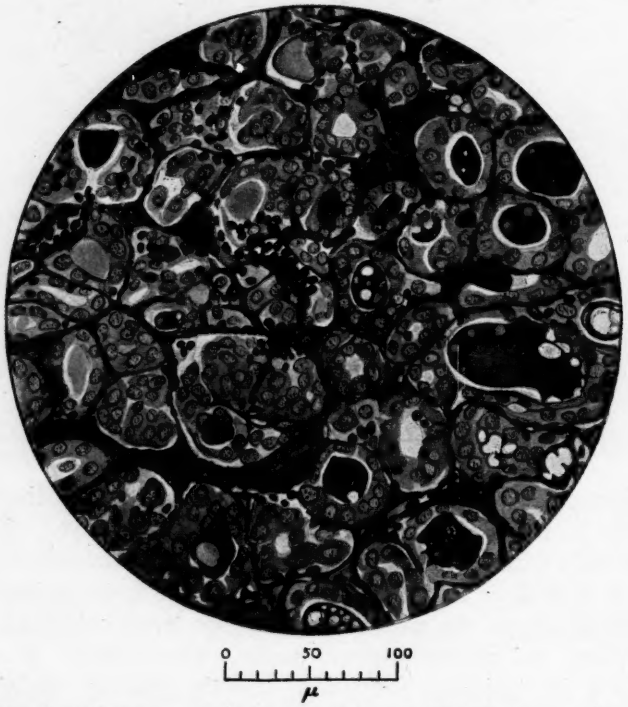

FIG. 275.—Hashimoto's struma. Part of section shown in *Fig.* 274, drawn under a higher power. The intervesicular lymphoid infiltration and the widespread changes in the thyroid epithelium are shown, as well as the dichroic staining of the remaining colloid. Stained Gallego. (× 220.)

Hashimoto states, correspond to Erdheim's granules (1903). According to Eisen (1936) rod-shaped mitochondria are to be found by Cowdry's method (1922) in the hypertrophic epithelial cells and in the syncytia of the lymphoid type of goitre which he includes with Riedel's disease, but which it is clear from his description corresponds to struma lymphomatosa. In cases which have been treated by iodine he believes there is evidence that these *mitochondria*, which he regards as criteria of cellular activity, are absent or represented by mere granules. Evidence of mitosis in the epithelial cells is conspicuous by its absence. There is considerable difference of opinion as to whether the epithelial cells show hypertrophy rather than mere hyperplasia. Shaw and Smith (1925) say that the cells are hypertrophic and

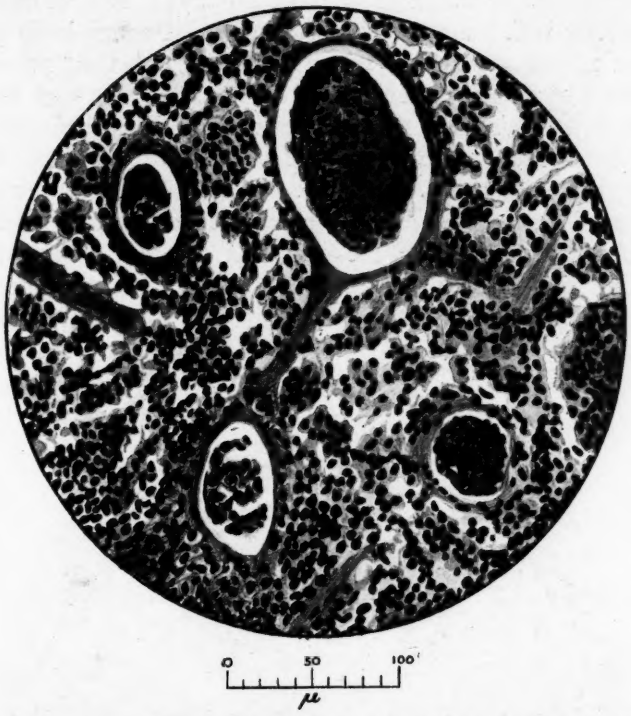

FIG. 276.—Hashimoto's struma. Section illustrating the intrafollicular masses of epithelial cells and the diffuse intralobular lymphocytosis. Stained H. & E. (× 220.)

show all the signs of increased functional activity, but that cellular degeneration keeps pace with the epithelial hyperplasia. Renton, Charteris, and Heggie (1938) deny the hypertrophic character of the epithelial cells and syncytia, asking why it is that these patients show *hypothyroid* and not *hyperthyroid* clinical features if there is even a moderate degree of epithelial hypertrophy. The answer would appear to be rather that the epithelial hypertrophy explains why a certain number of patients exhibits no hypothyroid phenomena, and also why in the early stages there may be a moderate elevation of the basal metabolic rate with transitory toxic symptoms such as wasting and tachycardia.

The *colloid* varies considerably in amount and in staining properties. It may be sufficient to cause flattening of the epithelial cells. Usually there are peripheral

and occasionally central vacuoles present in the colloid. The staining reaction varies from vesicle to vesicle (*Fig.* 275); it may be normal and eosinophil, there may be patchy basophil areas, or it may be entirely basophil. It may also be granular rather than homogeneous. Usually the colloid is much reduced in amount, and frequently absent altogether, though isolated masses surrounded by foreign-body giant cells or within lymph-spaces occur in some specimens.

Plugs of epithelial cells are common within the colloid-free vesicles (*Fig.* 276). Such cells may retain their cell walls and staining characters or they may be shrunken or completely desquamated. Mononuclear wandering cells in varying numbers may also be found within the vesicle, as well as unmistakable plasma cells.

3. The Connective Tissue.—This is everywhere increased in amount, showing up well with van Gieson's or Mallory's stain (*see Fig.* 274). It is widely infiltrated with lymphocytes, among which are a few plasma cells. Foreign-body giant cells were present in about 10 per cent of my own material, though their presence or absence cannot be regarded as pathognomonic since they may be met with in many forms of non-suppurative thyroiditis (Lee, 1935, de Quervain and Giordanengo, 1936), though rarely if ever in Riedel's disease. Giant cells, when present, have eosinophil protoplasm, are rounded, ovoid, crescentic, or irregular, with the nuclei arranged peripherally, their long axes tangentially or radially orientated, though not uncommonly the nuclei are grouped in the centre of the cell or are quite irregularly distributed. The role of these giant cells is, as Olper (1935) showed, the elimination of colloid which cannot be otherwise absorbed, and it must be assumed that

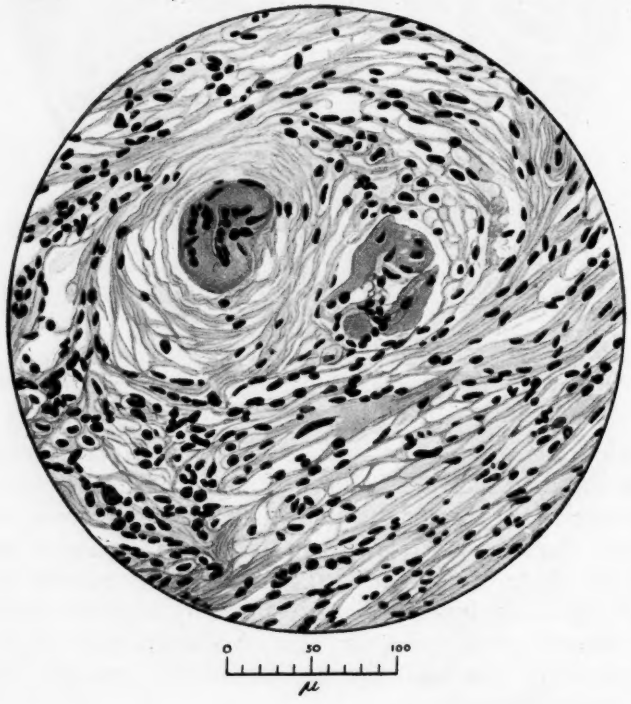

FIG. 277.—Riedel's disease. Section from specimen shown in *Fig.* 267, illustrating the adult character of the fibrous tissue, and the almost entire absence of remnants of thyroid vesicles. Stained H. & E. (× 220.)

FIG. 278.—Riedel's disease. Section from another part of the specimen shown in *Fig.* 267, near the periphery of the fibrous mass, illustrating the process of strangulation of the thyroid vesicles. Stained H. & E. (× 220.)

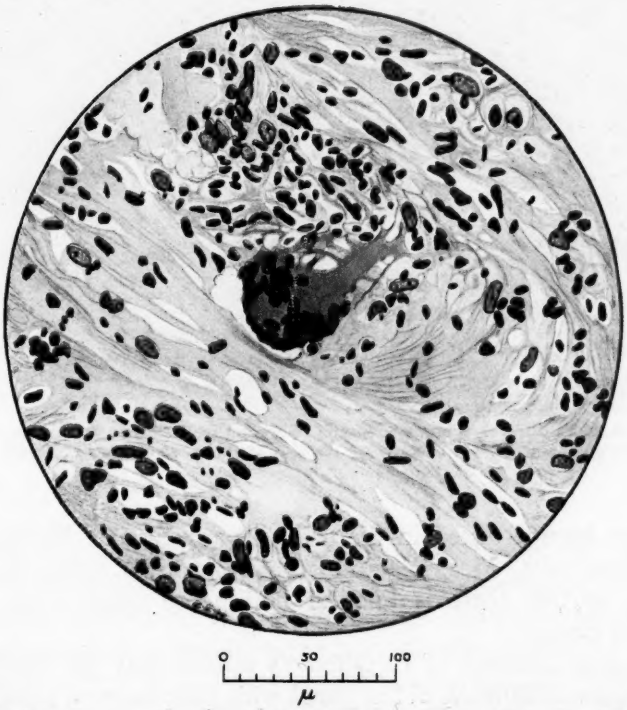

FIG. 279.—Riedel's disease. To show foreign-body type of giant cell (rare). Stained H. & E. (× 220.)

whereas in certain types of chronic thyroiditis the elimination of colloid by normal methods is so defective that many new giant cells arise for the purpose, in Hashimoto's struma there is seldom any necessity for the intervention of such cells and in Riedel's struma even less so. It is very doubtful indeed, therefore, whether a distinct 'foreign-body giant-cell' type of thyroiditis need be split off as Lee has done.

4. The Blood-vessels.—These are little altered in size or structure, and endarteritis is not met with in struma lymphomatosa. No micro-organisms, spores,

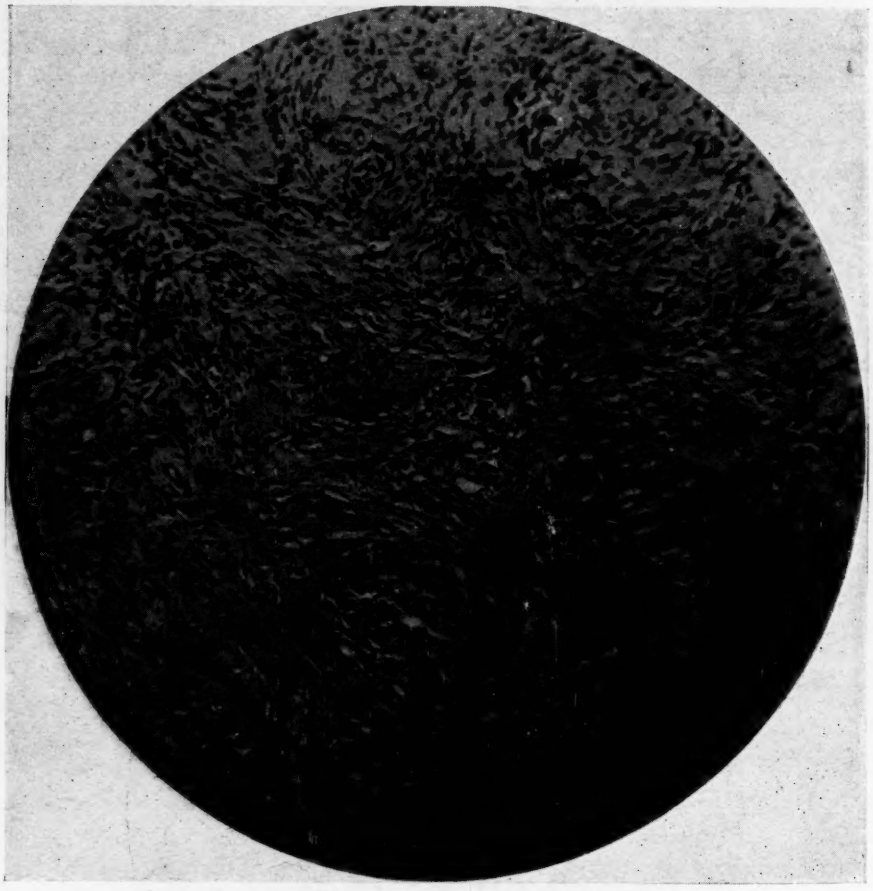

FIG. 280.—Riedel's disease. Photomicrograph of section from fibrous part of specimen illustrated in *Fig.* 264. There is no trace of epithelial structures. (× 50.)

or protozoa have been detected in the gland in any case of Hashimoto's struma, nor have the usual tests, bacteriological or biological, for tuberculosis or syphilis proved positive, so that there is little or nothing to connect the disease with a micro-organismal cause.

The histological features of Hashimoto's struma may be briefly summarized thus: (1) Abundant infiltration of the gland with lymphocytes, together with many active germ follicles. (2) Profound changes in the vesicular epithelium, with

eventual disappearance of colloid. (3) Widespread new formation of connective tissue.

Comparison with Riedel's Disease.—Contrasted with this, Riedel's disease is characterized by the *absence of diffuse lymphocytic infiltration* and of lymph-follicles, though, as in every other form of goitre, an occasional lymph-follicle may be seen even in Riedel's disease, in which usually they are entirely wanting. The changes in the *parenchyma* are of a totally different nature. For the most part there are no traces of epithelium or colloid throughout the extirpated tissue

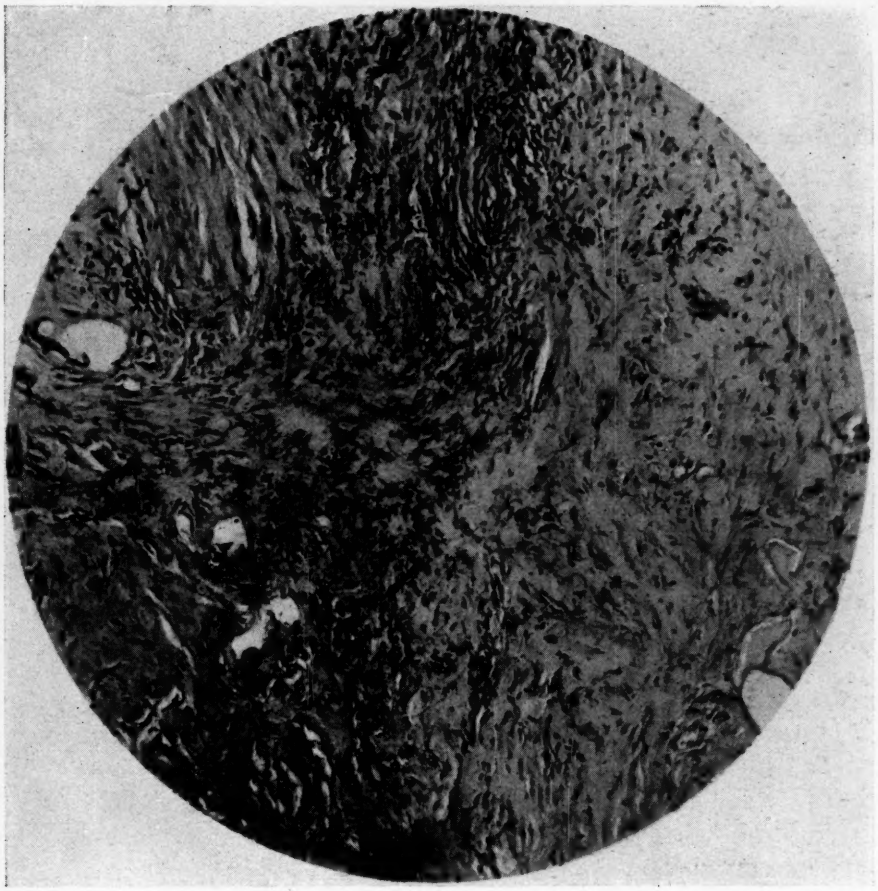

FIG. 281.—Riedel's disease. Photomicrograph of the peripheral tissue shown in *Fig.* 265. Note extensive hyalinization. (× 50.)

(*Fig.* 277), but at the periphery there are small groups of shrunken vesicles surrounded by dense fibrous tissue which has the appearance of strangling them (*Fig.* 278). Giant cells are very rarely seen (*Fig.* 279), but their presence cannot be allowed pathognomonic significance. Immediately outside the fibrotic area are to be seen well-formed vesicles containing normal colloid, and having all the appearances of being in full functional activity, a condition reflected in the fact that evidence of hypothyroidism either before or after operation is unusual. The bulk

of the new tissue in Riedel's disease is composed of adult fibrous tissue (*Fig.* 280) often relatively poor in cells and extensively hyalinized (*Fig.* 281), though at the periphery of the mass some fibroblasts are often visible, contrasting thus with the forms of non-suppurative thyroiditis described by de Quervain and Giordanengo in which the tissue in certain areas is rich in cells, œdematous, and only partly cicatrized. On the surface of the mass, striped-muscle cells can be seen infiltrated by fibrous tissue continuous with that in the thyroid.

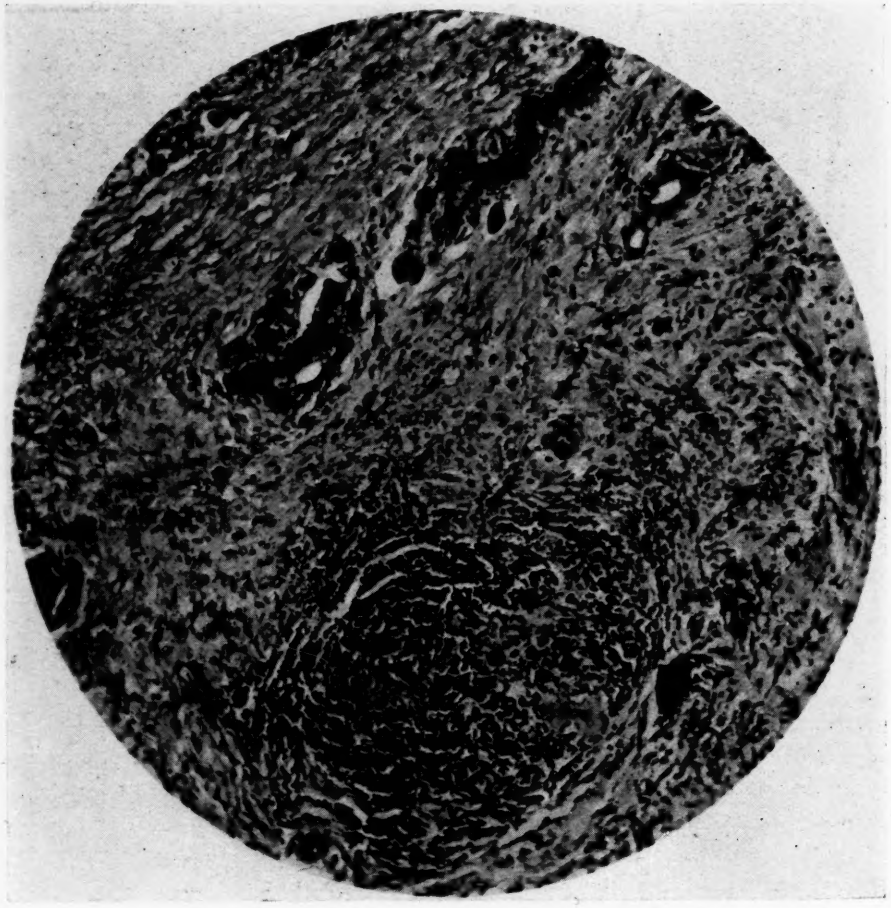

FIG. 282.—Photomicrograph of a gumma of the thyroid gland. (× 120.)

In *syphilis* of the thyroid there is usually well-marked endarteritis in the blood-vessels and evidence of necrosis both macro- and microscopical, the parenchyma suffering very much as in Riedel's disease (*Fig.* 282).

In *tuberculosis* the characteristic organism may be detectable, and there is little indication of the advanced fibrosis seen both in Riedel's disease and in chronic non-specific thyroiditis, many of the vesicles at the edge of the caseous tissue containing healthy looking colloid (*Fig.* 283).

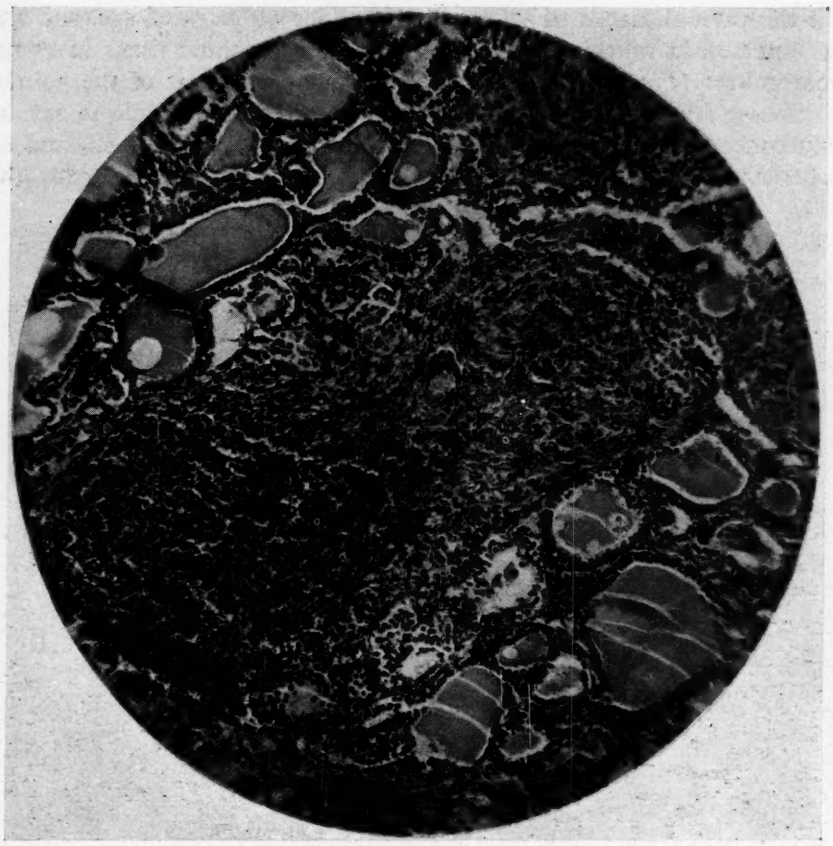

FIG. 283.—Photomicrograph of caseous tuberculosis of the thyroid. (× 120.)

PATHOGENESIS AND AETIOLOGY

The nature of the lesion in Hashimoto's disease is quite obscure, and it is mere obscurantism to refer to it as an inflammatory condition. It is clear from a study of the clinical histories of the proved cases that the goitre rarely if ever follows on an attack of one or other of the acute inflammatory diseases, nor does it exhibit any of the recognized features of an inflammatory state throughout its course. Histologically it reveals none of the varied pictures which de Quervain and Giordanengo (1936) have so fully and convincingly described for the several types of thyroiditis and strumitis. It is true, however, that Brünger (1915) and Eason (1927) regard the presence of lymphoid follicles in the thyroid as evidence in itself of an inflammatory process.

The source of the lymphoid infiltration is easier to account for than is the stimulus which induces it. It is unusual to find definite lymphoid aggregations in the normal thyroid gland, yet I have one or two histological preparations which exhibit it (*Fig.* 284). Poer, Davison, and Bishop (1936), on the contrary, deny that *germinal* lymphoid follicles are ever found in the normal thyroid gland. Simmonds (1913), working with autopsy material from Karlsruhe, found lymphoid collections in 5 per cent of apparently healthy thyroid glands. Such lymphoid foci did not

occur in the thyroid glands of young people under 30 years of age, and were five times as common in women as in men. He found lymphoid tissue in 15 per cent of simple goitres (*Figs.* 286, 287) as well as in 75 per cent of the goitres from Graves' disease (*Fig.* 285), and he concludes that it is impossible to say whether the disturbance leading to lymphoid infiltration is general or local, and again if local whether it is chemical, mechanical, or inflammatory. He adds that the

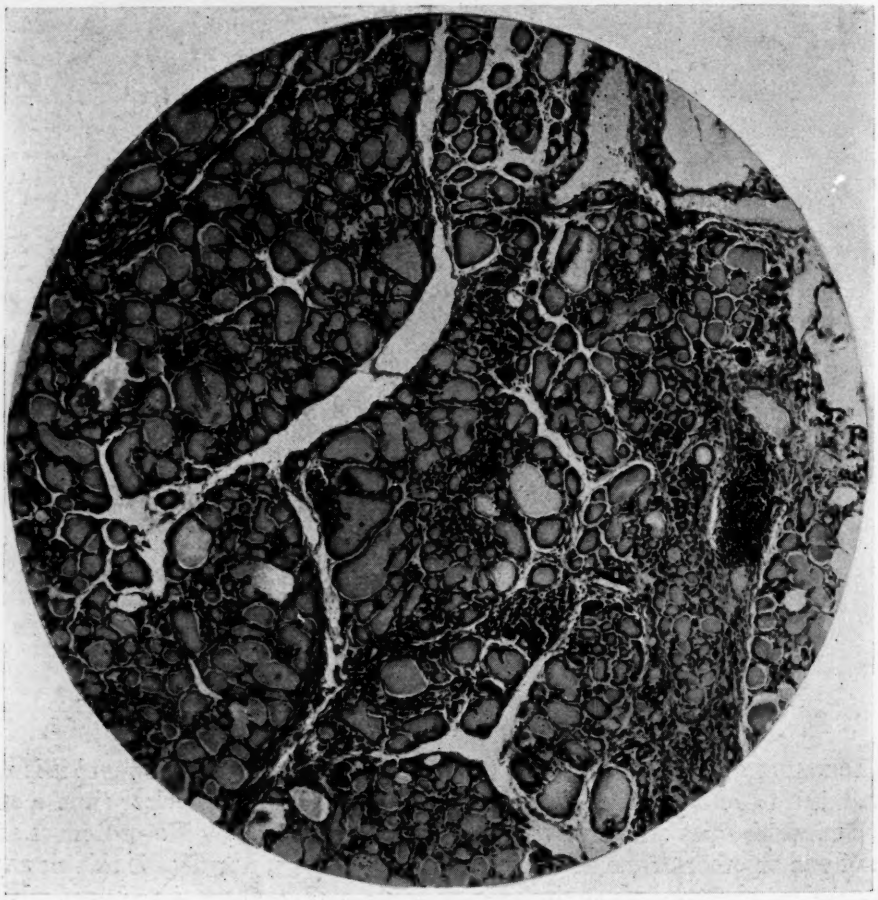

FIG. 284.—Photomicrograph of normal thyroid gland from a healthy female, aged 30. One small lymphoid accumulation is seen. (× 50.)

quantitatively and qualitatively altered secretions in Graves' disease may be a sufficient chemical stimulus to the formation of lymphoid tissue, as also may be iodine medication. In a later paper Simmonds (1923) describes changes in the thyroid glands of elderly obese patients resembling in certain particulars those of Hashimoto's struma, especially in the tendency to lymphoid infiltration and subsequently to destruction of the epithelial elements, terminating in myxœdema. These were, however, atrophic glands, and it appears to me impossible to look upon the processes as essentially similar. On the one hand there is the small or shrunken gland described by Simmonds; and on the other the goitrous gland of

Hashimoto, which may within a few weeks reach a very considerable bulk. At operation the lymphoid tissue appears not merely to be replacing something

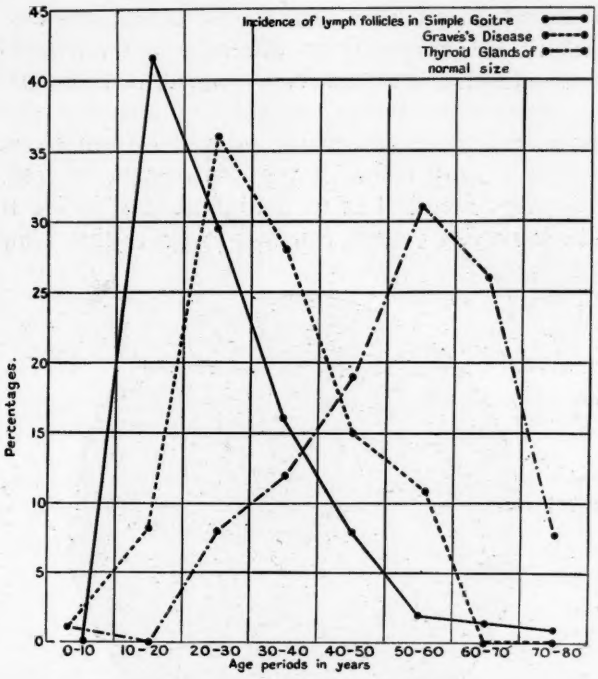

FIG. 285.—Relative frequency of lymphoid follicles in simple goitre, Graves's disease, and normal thyroid gland. (*From Simmonds.*)

FIG. 286.—Photomicrograph of lymph-follicle in simple nodular goitre. (× 29.)

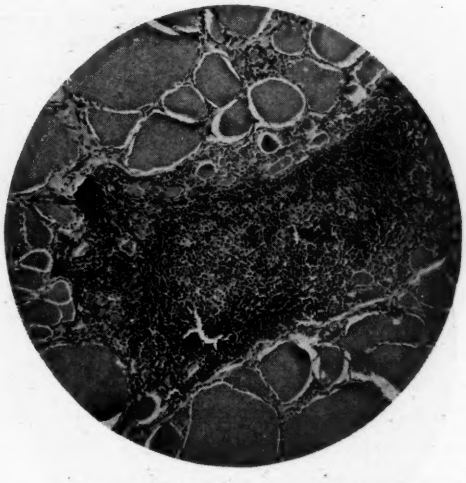

FIG. 287.—Nodular goitre. Photomicrograph of lymph-follicle with germ centre. (× 67.)

which has undergone shrinkage, but to possess enormous intrinsic activity, so that the tension within the gland in the prefibrotic stage is considerable, the pallid tissue bulging visibly when the capsule is incised.

Several authorities, e.g., von Werdt (1911), Reist (1922), Payr (1927), Kreuzbauer (1930, 1931), Boyden, Coller, and Bugher (1935), and Dunhill (1937), lay emphasis on the possible influence of iodine medication on the development of the lymphoid infiltration of Hashimoto's struma as well as the similar but focal changes so frequently seen in thyrotoxic goitres (*Figs.* 288–292), but it should be remembered that in Hashimoto's cases there had been no iodine medication and the same remark applies to 17 cases in my own series. It is also true that large focal areas of lymphoid infiltration may be discovered in goitres from Graves' disease which were removed in this country before it was the custom to treat such cases with iodine. Jaffé is also very sceptical as to the influence of iodine therapy in struma lymphomatosa. It is not, of course, essential to prove that lymphoid follicles are

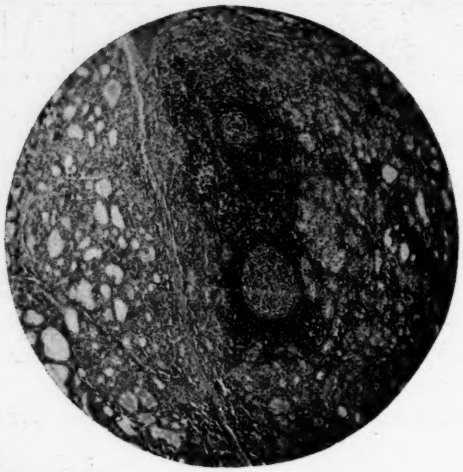

FIG. 283.—Photomicrograph from a case of primary thyrotoxicosis showing lymphoid infiltration of 'focal type'. (× 27.)

FIG. 289.—Photomicrograph from a case of primary thyrotoxicosis to show diffuse lymphocytic infiltration. (× 74.)

FIG. 290.—Photomicrograph from a case of primary thyrotoxicosis. Streaky lymphocytic infiltration. (× 27.)

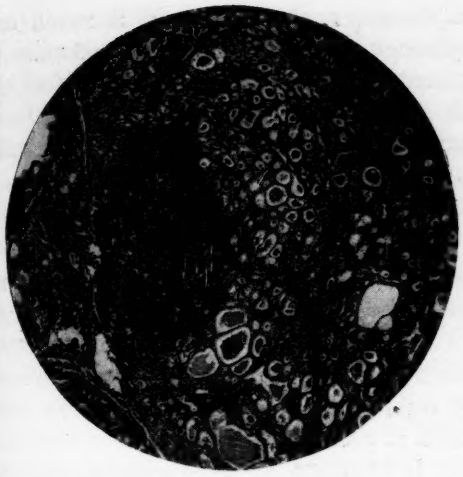

FIG. 291.—Photomicrograph from a case of recurrent primary thyrotoxicosis, showing large pseudo-follicle. (× 27.)

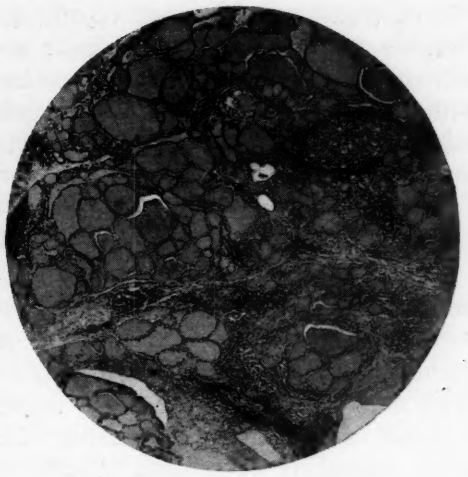

FIG. 292.—Photomicrograph from a case of secondary thyrotoxicosis, showing a follicle and streaky infiltration. (× 27.)

present in the normal thyroid gland in order to account for the various lymphoid infiltrations met with in simple goitre, in thyrotoxicosis, and in Hashimoto's struma, since undifferentiated mesenchymal cells and possibly also reticulum cells are to be found widely scattered in the stroma of the thyroid. This accords with Maximow's views (1924) on the potentialities of the mesenchyme, which thus may provide an intrinsic source for the development of lymphoid tissue, an origin the more likely as there is so little to indicate any spread of lymphoid changes into the thyroid from without.

Hashimoto compares struma lymphomatosa and Mikulicz's disease, but there appears to be no evidence that they are in fact related, and little, if any, similarity histologically between the two lesions.

Graham (1931) does not exclude the possibility of a relationship to lymphosarcoma (*Fig.* 293), but although he thinks that he has seen at least one case exhibiting a transition from Hashimoto's struma to sarcoma, no such development has appeared in any of my own series, some of which have been followed up for nearly twenty years.

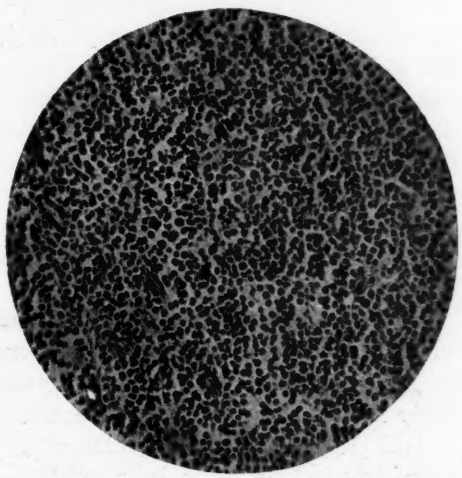

FIG. 293.—Photomicrograph from a case of reticulum-cell sarcoma of the thyroid in a woman aged 38. (× 110.)

Williamson and Pearse (1929) look upon struma lymphomatosa as occurring in physiologically subnormal thyroid glands undergoing compensatory hyperplasia and deny its granulomatous character. They associate the condition with the 'lymphogenic secretion' of the gland, which they claim is free from thyroxin, and maintain that the lymphocytic infiltration picks out the 'specific thyroid lymph-spaces' in a selective fashion.

Wilson (1927), and Rienhoff (1929), have, however, shown that Williamson and Pearse's description of the ultimate morphology of the thyroid gland cannot be substantiated. Little therefore is to be gained by pursuing such a concept of the pathogenesis of Hashimoto's struma, which in effect appears to be neither inflammatory, neoplastic, nor degenerative in any way comparable with what is usually understood pathologically by such terms.

CLINICAL FEATURES OF HASHIMOTO'S STRUMA

1. History and Mode of Onset.—There is nothing in the series of cases under review to confirm Eason's (1927–28) view that struma lymphomatosa and Reidel's disease are late developments in a thyrotoxic type of goitre. Since 1928, when Eason raised the question, I have taken pains to inquire into this possibility in all such cases, with consistently negative results. It is in fact striking how little evidence there is of any pre-existing ill health in patients with Hashimoto's struma, either immediate or remote. Unlike what is common in most non-suppurative forms of thyroiditis and strumitis, there is seldom any preceding acute illness or other toxic or infective state, general or local. Fatigue, shortness of breath, and increase in weight are common symptoms, but they can legitimately be ascribed partly to direct pressure and partly to the hypothyroid tendencies so often revealed when the basal metabolic rate is estimated. It cannot be denied that certain toxic features may also occur in exceptional cases, exemplified by loss of weight, nervousness, and a moderate elevation of the basal metabolic rate, but these are explicable in relation to the degree of dyspnœa which exists and to the hypertrophic changes in the thyroid epithelium, which, however, are comparatively short-lived. In other words, toxic features do not precede the disease, though they may be associated with its onset, in which event they have no tendency to become aggravated or to lead to the complete picture of thyrotoxicosis, primary or secondary. There are of course many cases of advanced thyrotoxicosis in which more or less of the hyperplastic tissue is replaced by a diffuse lymphocytic infiltration among which there may be many germinal centres. These changes are, however, essentially focal, and considerable areas of actively hyperplastic colloid-bearing tissue invariably coexist with the lymphoid areas (*see Figs.* 288–292), indicating that it is a secondary phenomenon, whereas in Hashimoto's struma the evidence is all in favour of the lymphoid change being primary.

In many cases the patient is a woman in the late forties or early fifties, inclined to obesity, with the facies of early myxœdema and a rather dry skin, and is apathetic or torpid in habit, with a basal metabolic rate which suggests a moderate or even fairly high-grade type of myxœdema.

In Riedel's disease evidence of thyrotoxicosis or of myxœdema is almost invariably lacking, though as in all conditions associated with severe dyspnœa and nocturnal asthmatic attacks, the basal metabolic rate may be moderately raised and the patient exhibit nervousness and loss of weight. In those exceptional and late cases in which both lobes are affected, evidence of hypothyroidism may be forthcoming even in Riedel's disease, but I have never personally seen one, though they are on record. Much the same applies to the non-suppurative form of thyroiditis and strumitis described so fully by de Quervain and Giordanengo, and for the same reason—namely, that in these lesions there is sufficient secretory tissue remaining to carry out normal thyroid activity.

There is very seldom any pyrexia or other evidence of inflammation at the onset of Hashimoto's struma, or for that matter in Riedel's disease, in spite of Clute and Lahey's (1932) view that the latter condition has an origin in acute thyroiditis, as undoubtedly is true for many other non-suppurative forms of chronic thyroiditis. The blood-picture is seldom altered, except for a mild degree of secondary anæmia in certain cases.

Localized pain and tenderness in the thyroid gland, as well as pain referred to the ear, nape of neck, and upper limb, are characteristic of acute and subacute thyroiditis, and particularly of the giant-cell type which Lee regards as an entity, but they do not occur in uncomplicated cases of struma lymphomatosa or in Riedel's disease. Headache, vertigo, and slight dysphagia may occasionally be complained of, but are unusual. The goitre develops, with certain striking exceptions, at a moderate rate, so that it may be months before it causes pressure symptoms, whereas in Riedel's disease it is more commonly a matter of weeks. Sometimes the goitre grows rapidly at first, followed by a slowing down, or it may steadily progress. Even in the largest goitres of Hashimoto's type there is seldom any evidence of pre-existing thyroid enlargement, except in those arising where goitre is endemic. In none of the cases in the series here reported does the disease appear to have been engrafted on an established goitre—colloid, nodular, or hyperplastic—though the prolonged history of goitrous enlargements in one or two instances might suggest that possibility.

FIG. 294.—Hashimoto's struma. Radiograph showing the moderate tracheal compression.

FIG. 295.—Riedel's disease. Radiograph showing the extreme tracheal compression.

2. Pressure Symptoms.—These are seldom prominent in Hashimoto's struma (*Fig.* 294) unless the goitre is exceptionally large, when the trachea may be subjected either to bilateral or to antero-posterior compression as revealed by appropriate radiographs. Usually the worst that happens is a moderate dyspnœa on exertion. Interference with swallowing is also most unusual. No instance of laryngeal paralysis occurred in the series of cases now under review, though some hoarseness and dysphonia of an intermittent character is often observed: this appears to be due not to interference with the function of the interarytenoid muscle, but to the mechanical effect of the very solid goitre, much of which lies behind the larynx.

In Riedel's disease, on the other hand, pressure effects dominate the picture and reveal themselves by intense dyspnœa often worse when lying down, suffocative

attacks, and nocturnal asthma, as well as persistent stridulous cough. Radiographs show displacement and compression of the trachea, which is confirmed by tracheoscopy, the lumen of the trachea being reduced to the merest chink (*Fig.* 295). Dysphagia is less common, but may be as severe as in advanced malignant disease of the thyroid, and unilateral recurrent laryngeal paralysis has been noted in several cases.

Bilateral laryngeal paralysis has not been recorded in any one of the 65 cases of Riedel's disease available for study; yet if it were true that the whole gland usually becomes involved, it must be obvious that such a complication might occasionally be expected. This is therefore a strong point in proof of the essential focal character of Riedel's disease. The intensity of the pressure symptoms, quite apart from errors in diagnosis, has often led the surgeon to attempt the hazardous project of removing the mass as an emergency measure, or into performing tracheotomy, sometimes with little or no relief owing to the extensive character of the tracheal compression.

3. Type of Goitre.—The goitre itself in Hashimoto's struma is usually of moderate size (*Figs.* 296–300), every part of the gland taking a share in the enlargement, so that the pyramidal lobe is often palpable as an entity. It is smoothly lobular, the irregularities on its surface being an exaggeration of those normal to the thyroid gland in health. In the earlier stages the gland is moderately firm, but hardly more so than in the hyperplastic goitre of Graves's disease, and it moves freely on swallowing. When fibrosis has developed the gland becomes firmly or toughly resilient, but never as hard as iron or wood, and while moving on swallowing may appear rather unusually tethered to the trachea. The pulsation of the carotid vessels is readily palpable posterolaterally, in which direction they are displaced by the growing gland.

In Riedel's disease the intense hardness and fixation of the relatively small and smooth mass are the features which distinguish the condition from all other thyroid

FIG. 296.—Hashimoto's struma. From a woman aged 43. Basal metabolic rate, −15 per cent.

FIG. 297.—Hashimoto's struma. From a woman aged 46. Basal metabolic rate, −26–34 per cent.

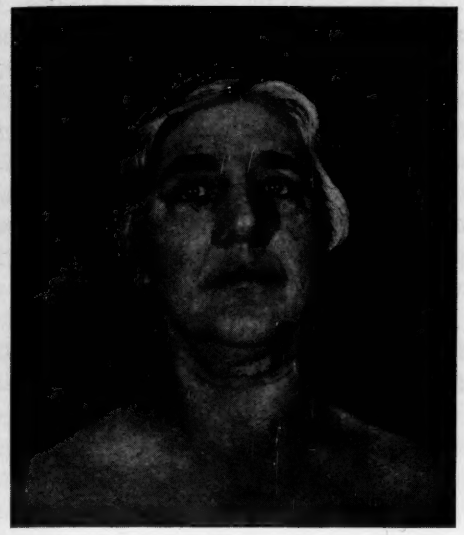

FIG. 298.—Hashimoto's struma. From a woman aged 60. Goitre twelve years, dyspnœa six months. Basal metabolic rate, – 30 per cent.

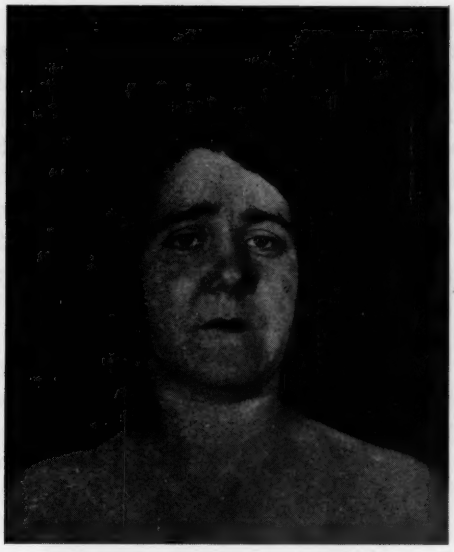

FIG. 299.—Hashimoto's struma. From a woman aged 43. Basal metabolic rate, – 40 per cent.

FIG. 300.—Hashimoto's struma. From a woman aged 50 with a basal metabolic rate of – 50. The thyroid enlargement is uniform and moderate. The features are heavy, resembling myxœdema.

lesions. In no form of malignant goitre is the mass so hard as in Riedel's disease, though that form of secondary growth following post-cricoid carcinoma approaches it closely in this respect. Movement on swallowing may be entirely abolished, and the surrounding structures cannot be separately palpated. The carotid artery on the corresponding side is usually completely obscured and its pulsations almost entirely obliterated. Such a state of affairs, though it may be met with in extensive and advanced malignant goitre, is not encountered in neoplasms of a size comparable with the mass of tissue in Riedel's disease.

4. Conditions met with at Operation.—In struma lymphomatosa the infrahyoid muscles and the surgical capsule of the thyroid gland are readily separable

from the latter, which can be dislocated from its bed with no greater difficulty than is met with in any of the more solid hyperplastic glands of primary thyrotoxicosis. Vascularity is slight and the main thyroid veins and arteries can be readily secured, though owing to the friability of the thyroid tissue the smaller intrathyroid blood-vessels are more difficult to control than in most goitres. On the whole the hæmorrhage encountered is less than in any other thyroid operation of comparable magnitude. Separation from the trachea is not difficult, for although the fibrous tissue binding gland to trachea is often markedly bulky and opaque, the plane of cleavage is never really obscured.

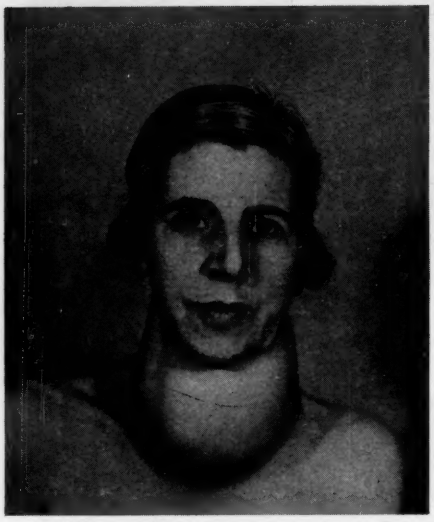

FIG. 301.—Reticulum-cell sarcoma of the thyroid in a woman aged 38. (*See Fig.* 293 for photomicrograph of tumour.) The large goitre contrasts with those characteristic of Hashimoto's struma.

In Riedel's disease the mobilization of the fibrous mass may prove a matter of the utmost difficulty. Many operations have had to be abandoned, others have proved fatal on the operating table from hæmorrhage, from suffocation, or from damage to vital structures, while yet in others it has been necessary to resect muscles, nerves, bones (such as the clavicle or portions of the sternum), the jugular vein, or common carotid artery, with dire consequences to the cerebral function, etc. Riedel describes how it took him two hours to extirpate a mass the size of a walnut after resecting the internal jugular vein: finally he abandoned the operation. It is always difficult to detach the infrahyoid muscles; consequently portions of them have as a rule to be extirpated with the main mass. Even more difficult is it to find any proper plane of cleavage which will enable the operation to be completed in an orderly fashion. If a blood-vessel be damaged it is extremely difficult to secure the bleeding point with artery forceps or even to under-run it with sutures. It is not easy to remove sufficient of the tissue to ensure relief from the pressure symptoms without risking encroachment on the great vessels of the neck, the trachea, or œsophagus, which are much more obscured than in malignant disease. It is often urged that the removal of a wedge of tissue from the region of the isthmus suffices to give relief, but a study of Riedel's cases does not increase one's confidence in this limited measure, since one of his patients died a few weeks later, one lived for fifteen months, and a third who survived for years was only partially relieved of his dyspnœa. It is in the subacute and chronic non-suppurative forms of thyroiditis described by de Quervain and Giordanengo that we have the conditions which enable relief to be secured by limited operations, and it is equally in this group that spontaneous regression is so common that in fact operative interference is seldom called for, except to correct a doubtful diagnosis of malignancy.

5. Hypothyroid Phenomena.—The progress of Hashimoto's struma even without operative treatment is towards myxœdema, as would be expected from its histology. I have had one such case (a woman now aged 62) under observation for some years, the diagnosis being sufficiently clear and symptoms of pressure so

trivial that it has been possible to avoid operative treatment. The basal metabolic rate fell from — 12 per cent to — 36 per cent during the first year and a half, and she now requires full doses of thyroid extract to maintain thyroid function. I have not observed any case of spontaneous retrogression such as undoubtedly occurs with the foreign-body giant-cell type of thyroiditis.

Sir T. Dunhill has reported an interesting case in his Lettsomian Lectures for 1937: At a first intervention the extirpated tissue proved to be so extensively infiltrated with lymphoid tissue that supervention of myxœdema was anticipated. The patient lost all her symptoms, yet some years later developed further thyrotoxic symptoms necessitating a second operation, the tissue removed at this intervention showing all the characteristics of a hyperplastic goitre modified by prolonged iodine therapy. In this case, however, the primary lesion was not Hashimoto's struma but thyrotoxicosis, and the reappearance of thyroid hyperplasia with the disappearance of the lymphoid infiltration is explicable on the ground that at the first operation a portion only of the gland was extirpated and therefore tissue free from lymphoid infiltration (and capable of hyperplasia) was almost certainly present in the part of the thyroid which was conserved.

It is extremely difficult to estimate the *rate of progress* in a disease with so few symptoms, but one of the largest goitres of the Hashimoto variety which I have seen reached its maximum in a few months, considerable dyspnœa resulting, whereas in those glands of more moderate size little advance may be observed in the course of a year or more.

In Riedel's disease progress is relatively more rapid, but once serious pressure effects arise the danger to the patient has little relationship to the actual size of the thyroid mass. There is good reason to doubt whether those cases recorded as having spontaneously retrogressed were in fact examples of Riedel's disease. It is probable that they were inflammatory lesions of the thyroid without the adult fibrous tissue and the perithyroid involvement so characteristic of Riedel's disease, the more so as inquiry into the after-history of my own series of cases of true Riedel's disease and a review of the literature reveals that recurrence or relapse is not unusual. Myxœdema, however, is rarely the outcome of Riedel's disease even after attempts at radical extirpation, a point in sharp contrast to what happens in struma lymphomatosa.

DIAGNOSIS

The difficulties in the diagnosis of Hashimoto's struma to a large extent are resolved when once its status *vis-à-vis* Riedel's disease is admitted. A firm goitre which appears in a middle-aged patient, usually a woman, reaches its maximum in a few months, and involves every part of the gland, causes only a moderate degree of dyspnœa, but produces neither serious pressure effects, thyrotoxic symptoms, pain, tenderness, pyrexia, nor other inflammatory phenomena, is almost certainly a struma lymphomatosa. If to these features be added the *absence* of any evidence of involvement of extrathyroid tissues and the *presence* of some degree of hypothyroidism, the diagnosis is placed beyond a peradventure.

Differential Diagnosis.—

1. *From Lymphosarcoma and other Malignant Neoplasms.*—From malignant disease the distinction is made by noting that in struma lymphomatosa all parts of the gland are affected, without serious encroachment on extrathyroid tissues, without

involvement of the main vessels and nerves, and without any trace of the irregular bossiness of the surface of the gland or of enlarged lymph-nodes. Nevertheless the conditions are frequently confused, for Emerson (1935), in reporting 9 cases of Hashimoto's struma, states that 5 were diagnosed as malignant goitre. This error has been made more frequently than might be expected, sometimes inducing the surgeon to perform complete thyroidectomy, an operation dangerously easy to carry out in struma lymphomatosa but rarely if ever feasible or desirable in malignant disease. In the latter it is extremely rare to find that the whole thyroid is involved without such a degree of infiltration of surrounding structures as to preclude the possibility of complete thyroidectomy.

The reaction of the goitre to radium therapy may also be employed to differentiate Hashimoto's struma, which is in fact remarkably radiosensitive.

From lymphosarcoma, into which Graham (1931) suggests it may become converted, struma lymphomatosa is distinguishable by the absence of involvement of regional lymph-nodes, as well as by the bulky goitre resulting from lymphosarcoma (*Fig.* 301).

2. *From Riedel's Disease.*—Diagnosis is made by a consideration of the numerous points of distinction elaborated elsewhere in this article, but which may be tabulated as follows :—

Table I.—Differential Diagnosis between Hashimoto's Struma and Riedel's Disease

	Hashimoto's Struma	*Riedel's Disease*
1.	Preponderates in women from 45 to 60 years of age	Occurs in younger men and women than does struma lymphomatosa
2.	There is a tendency to myxœdema	There is little tendency to myxœdema except after radical operations
3.	All parts of the thyroid gland are involved, but nothing outside it. The goitre is sometimes large but never woody hard	The disease is usually unilateral with extension to extrathyroid structures. The goitre is small, intensely hard, and smooth.
4.	Pressure effects are seldom severe	Grave pressure effects are the rule
5.	The histological structure, which varies with the stage of the disease, is characteristic	The mass is formed of dense scar tissue

3. *From Chronic Thyroiditis, Non-specific and Specific.*—From chronic thyroiditis of the giant-cell type described by de Quervain and Giordanengo, it is distinguishable by the absence of inflammatory symptoms throughout, by its bilateral character, the tendency to hypothyroidism, and the absence of any tendency to spontaneous cure.

From specific forms of chronic thyroiditis, i.e., tuberculosis, syphilis, and actinomycosis, it is differentiated by the absence of evidence of the specific causal organisms and of the special physical characters of the thyroid enlargement in these several diseases.

From calcified goitres of various kinds it is differentiated by radiographic evidence of the presence of this type of degenerative change.

TREATMENT

The main indications for treatment are: (1) To establish the proof that the condition is not a malignant neoplasm; and (2) To relieve pressure symptoms.

It has already been pointed out that diagnosis is usually possible even without recourse to a biopsy, though the latter step is so easy to carry out and so free from risk that it may be argued reasonably that it is almost essential in order to avoid dangerous error. The naked-eye appearances of the gland, once it is exposed, are usually sufficiently characteristic to permit confirmation of the diagnosis without waiting for microscopical examination, though with modern methods the delay of a few minutes necessary for such further confirmation is amply justifiable.

In order to relieve pressure a bilateral resection is usually called for, and it will be obvious from what has already been described that in many cases the 'circular' character of the goitre calls for full dislocation of the lateral lobes in order to enable this bilateral resection to be carried out on a scale sufficient to relieve the antero-posterior tracheal compression which exists in such cases. It is of course clear that the more radical the operation, the sooner will the patient exhibit hypothyroid phenomena—or if indeed such already exist, the more rapidly will they reach that of high-grade myxœdema. The advent of hypothyroidism is, however, sooner or later almost inevitable, and it cannot be a matter of great moment, once this has appeared, whether the patient has to take a small or a large dose of thyroid extract. It is, however, neither necessary nor desirable to perform complete thyroidectomy, an operation which is perhaps easier technically in struma lymphomatosa than in any other form of goitre with which I am acquainted. I have examined several museum specimens which illustrate this dangerous facility, dangerous not because of the inevitable myxœdema which in any case is only precipitated by such excessively radical methods, but because of the risk of damage to the parathyroid function as well as to the recurrent laryngeal nerves. Gilchrist (1935) quotes a case in which both myxœdema and tetany followed complete thyroidectomy in struma lymphomatosa, and I know of other similar cases. It is perhaps wise to avoid the ligation of the main thyroid vessels in carrying out the necessary extirpation, and this is rendered all the easier since the blood-supply is not sufficiently rich to make arterial ligation necessary on technical grounds.

There is very little risk or difficulty in carrying out what is necessary to relieve pressure in these cases, and in my own series as well as those quoted by Graham (1931), McClintock and Wright (1937), and others, the operative risk proved negligible. This is in striking contrast to what is found in Riedel's disease, in which radical operations even if attempted have rarely been completed, although to achieve them the cervical muscles, the clavicle, and the sternum have been divided and the great vessels, the vagus, the thoracic duct, trachea, and œsophagus have been resected or accidentally damaged and tracheotomy has often proved necessary; as would be expected, the immediate mortality is high.

1. **Surgical.**—It is a matter of considerable doubt as to whether surgical treatment is necessary in Hashimoto's disease, assuming that pressure symptoms are slight. Avoidance of resection will undoubtedly postpone the necessity for thyroid medication, and there are some who believe that the disease in certain cases may either cease to progress to the stage of thyroid deficiency or may even retrogress, though the evidence for this is very slender.

2. Radium Therapy.—Very recently radium therapy has been shown by Renton, Charteris, and Heggie to be almost a specific for the type of goitre which is here identified as struma lymphomatosa and which appears to be exceptionally radiosensitive. These authors give valuable details as to dosage, etc., and point out that the method affords a rapid differential test from malignant disease of the thyroid, which is in general much less radiosensitive, though this does not apply to lymphosarcoma. McEwan, of Bradford, informs me that he has also had a case which cleared up rapidly under similar methods. It will also be recalled that in one of the cases to which Ewing referred the goitre disappeared under radium therapy. Similar successes have been claimed for radium therapy in true Riedel's disease, but it is extremely unlikely, bearing in mind the pathological nature of the tissue in this condition, that any form of radiotherapy could result in absorption of the adult fibrous tissue which bulks so largely in it, and it seems more reasonable to assume in the cases classified as successes for this method of treatment that the lesion was either of the Hashimoto type or one or other of the various types of non-suppurative thyroiditis.

3. X-ray Therapy.—There seems little reason to doubt that X-ray therapy also, if of only sufficiently high voltage, would affect struma lymphomatosa favourably, though Boyden, Coller, and Bugher (1935), and Portmann (1932), disapprove of it in such cases, while Means (1937) advocates its use.

Definite successes for X-ray therapy in Riedel's disease have been claimed by Bayon (1904), by Silatschek (1910), and by Maloney (1930), but the evidence is in favour of the view that the cures effected were in connexion with certain forms of subacute and chronic non-suppurative thyroiditis rather than with true Riedel's disease, in which the histological character of the pathological tissue argues strongly against it being sensitive to X-ray therapy of whatever wave-length the latter might be.

PROGNOSIS

1. Tendency to Myxœdema.—If untreated, struma lymphomatosa may pass into myxœdema, the transition being so gradual that, unless repeated basal metabolic rate estimations be made, it is often overlooked. No medical treatment appears to have any effect whatever, and spontaneous regression in typical Hashimoto's disease has not so far been proved to occur, though it is arguable that it has in fact occurred whenever the patient fails to exhibit hypothyroid phenomena after a period of years. After bilateral resection of a part of both lobes complete and permanent relief of pressure symptoms is to be anticipated even if the onset of hypothyroid phenomena is thereby hastened. Complete restoration to health was noted to be slow by Hashimoto, but this no doubt was due to failure to recognize that thyroid medication should be commenced early whenever there is reasonable ground for assuming that otherwise hypothyroidism would supervene.

2. Relapses.—Recurrence after operation is most unusual, and when it occurs is due usually to the bilateral nature of the goitre not having been recognized, resulting in a unilateral resection which fails to relieve pressure adequately, thus necessitating a further intervention on the contralateral side. It is a mistake in these cases to assume that the disease has in the interval merely spread from one lateral lobe to the other, for which view there is no reliable evidence: the explanation is most probably that in certain asymmetrical goitres (based on congenital asymmetry

of the thyroid gland) one large lateral lobe may so overshadow the other smaller lobe that the latter is allowed to remain undisturbed, and the fact that it is equally affected pathologically is not recognized. This appears to be the explanation of several of the cases in which second operations were called for at intervals of from one to four years; it was certainly so in the one case early in my own series which required a second intervention.

3. Post-operative Complications.—These are very unusual, unlike what happens after attempts to extirpate the tissue radically in Riedel's disease. Laryngeal paralysis (*but see* Clute, Eckerson, and Warren) and tetany are both rare following operations for struma lymphomatosa except in the cases to which attention has already been called, in which complete thyroidectomy had been performed in the erroneous belief that the condition was malignant. Post-operative myxœdema is to be expected sooner or later; it occurred in 64·8 per cent of the series here reported, as well as in 78·8 per cent of the cases reported by McClintock and Wright.

In my own series a daily dose of 1–3 gr. of thyroid extract (based on the dry gland) has proved adequate to control the hypothyroid symptoms. At present there is insufficient evidence to indicate whether after radium or X-ray therapy there is the same tendency to the supervention of myxœdema, as in Renton, Charteris, and Heggie's series no estimations of the basal metabolic rate appear to have been made, but nevertheless these authors state that no hypothyroid phenomena were detected though one of their cases was followed for as long as five years. By contrast the prognosis in Riedel's disease is less favourable, as has already been suggested by reference to the poor results which Riedel himself recorded. In one of my own cases which passed out of my control, pressure symptoms recurred within a year or so, and the patient died of asphyxial symptoms four years later; in a more recent case stridor and dysphagia recurred within a few weeks, necessitating tracheotomy which afforded some relief. Traum (1931) admits the failure of radical extirpation to relieve pressure symptoms, as is indicated by the fact that in several cases recorded in the literature tracheotomy was eventually called for (Monod and Monod, 1923); in others such complications as secondary hæmorrhage from the carotid (Tailhefer, 1898; Delore and Alamartine, 1911; St. George, 1924), hemiplegia (Tailhefer, 1898), thoracic duct fistula (Ricard, 1901), pneumothorax (Meyer, 1913), pneumonia, and recurrent pharyngeal paralyses have occurred, indicating clearly the amount of trauma which has been inflicted on the tissues during the attempt to extirpate enough of the constricting mass to give relief from pressure. The immediate mortality is in the neighbourhood of 20 per cent, compared with none at all in my own series of struma lymphomatosa.

SUMMARY AND CONCLUSIONS

1. A series of 81 unpublished cases of Hashimoto's struma have been analysed in order to establish its specific features as compared with Riedel's disease and with certain other non-suppurative lesions of the thyroid gland.

2. The pathological features which characterize the disease are shown to be a diffuse lymphocytic infiltration associated with the presence of germinal lymph-follicles, a widespread though peculiar destruction of the thyroid parenchyma followed by fibrosis of a particular distribution. Somewhat similar changes of a *focal* type in thyrotoxic and other goitres are not accompanied by the clinical features of struma lymphomatosa.

Table II.—SUMMARY OF DATA RELATING TO HASHIMOTO'S DISEASE AND RIEDEL'S STRUMA

		HASHIMOTO'S STRUMA		RIEDEL'S STRUMA	
		McClintock and Wright (July, 1937) (47 cases)	Author (81 cases)	McClintock and Wright (60 cases)	Author (5 cases)
Sex	Male	4·2 per cent	3·7 per cent	18·2 per cent	20 per cent
	Female	95·8 per cent	96·3 per cent	81·8 per cent	80 per cent
Age	Youngest	26 years	10 years	23 years	27 years
	Oldest	75 years	74 years	78 years	62 years
	Average	49·2 years	57·6 years	40·3 years	44·4 years
Duration of symptoms	Shortest	30 days	1 month	15 days	3 weeks
	Longest	6 years	8 years	2 years	1 year
	Average	1·3 years	1·7 years	7·5 months	6·1 months
Duration of goitre	Shortest	3 days	3 weeks	14 days	3 weeks
	Longest	16 years	30 years	23 years	8 years
	Average	4·2 years	4·2 years	3·5 years	1·9 years
Thyroid involvement	Unilateral	100 per cent	100 per cent	30·5 per cent	80 per cent
	Bilateral			69·5 per cent	20 per cent
Pre-operative function	Thyrotoxic	0 per cent	0 per cent	Not stated	None
	Hypothyroid	Not stated	35·2 per cent	Not stated	None
Operative findings	Diffuse extrathyroid involvement	0 per cent	0 per cent	100 per cent	100 per cent
Post-operative function	Hypothyroid	78·8 per cent	64·8 per cent	27 per cent	20 per cent

Summary of data relating to Hashimoto's struma (author's cases, 51; communicated, but previously unpublished, 30; none of these appear in McClintock and Wright's series) and Riedel's disease (5 cases unpublished, not included in McClintock and Wright's figures).

3. Clinically struma lymphomatosa is associated with a tendency to progressive destruction of the thyroid function leading to myxœdema. The goitre itself affects all parts of the gland proportionally, and while firm and resilient never becomes iron hard or woody in consistency. There is never any diffuse extrathyroid involvement of the cervical tissues. Pressure effects tend to be slight or moderate in degree, in contrast to the grave pressure effects of Riedel's disease.

4. Diagnosis from malignant disease, Riedel's struma, and other forms of thyroiditis is frequently possible.

5. Surgical treatment is seldom imperative and should be avoided until the effects of radiotherapy have been determined. If operation is required, bilateral symmetrical partial resection of the gland without ligation of the main arterial trunks is probably the wisest course.

6. The operative risks are extremely small, the technical difficulties trivial, and post-operative complications rare, in contrast to the high mortality and morbidity associated with operations for Riedel's disease.

7. Recurrences are rare in struma lymphomatosa, though post-operative myxœdema must be anticipated and prevented by appropriate thyroid medication. Recurrences after operations for Riedel's disease are comparatively common, though post-operative myxœdema is exceptional.

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FRACTURES OF THE LOWER LEG
A METHOD OF REDUCTION AND IMMOBILIZATION

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THE most simple technique, consistent with efficiency, is always the most satisfactory in fracture work—and for that matter in all branches of surgery. The following apparatus and the method of using it for reducing and immobilizing fractures of the lower leg embody both these principles.

A description of the apparatus is unnecessary as the photographs (*Figs.* 302–304) are self-explanatory. It can be used with any modern table, provided there is some system for raising the table gradually. When the patient has been arranged with legs flexed over the end of the table, the Kirschner ' horseshoe ', which secures the wire in the calcaneus of the broken leg, is attached to the adjustable stirrup by

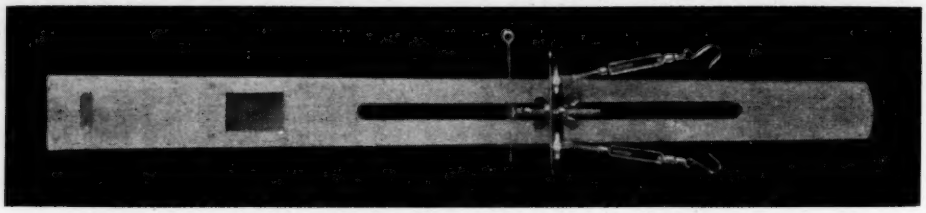

FIG. 302.—The apparatus. (*Down Bros. Ltd.*)

two steel hooks. This will be clearly seen in the photograph (*Fig.* 303), which also shows how the apparatus is fixed by the leg of the operating table, standing in a slot made for the purpose, thus allowing the stirrup end of the instrument to swivel into any desired position.

Only a few minutes are required to prepare for setting the fracture. The table is slowly raised by an assistant under the direction of the surgeon, who sits opposite the fractured limb. By palpation and comparison with the other leg, which is hanging in the same position, it is found that very little manipulation is required to obtain an almost perfect reduction. By means of a butterfly screw on the adjustable stirrup the foot (and therefore the lower fragment) can be quickly fixed in the correct position in relation to the upper fragment, which can be judged by observing the position in the sound limb. Likewise inversion or eversion of the foot may be altered as required, by two screws on either side of the stirrup. The leg is in the optimum position for the easy application for a well-fitting plaster, and slight pressure on the inner side of the setting plaster allows for the normal bowing of the tibia. If the fracture is in the upper two-thirds of the tibia, a second Kirschner wire may be put through the tibial tubercle and incorporated in the plaster, thus fixing the upper fragment and leaving a freely movable knee-joint. As can be easily seen from the free position of the leg, X-ray control is simple, using any portable apparatus. It has been found, however, that excellent results have been obtained when radiological aid has not been available, as comparison with the sound leg affords much help.

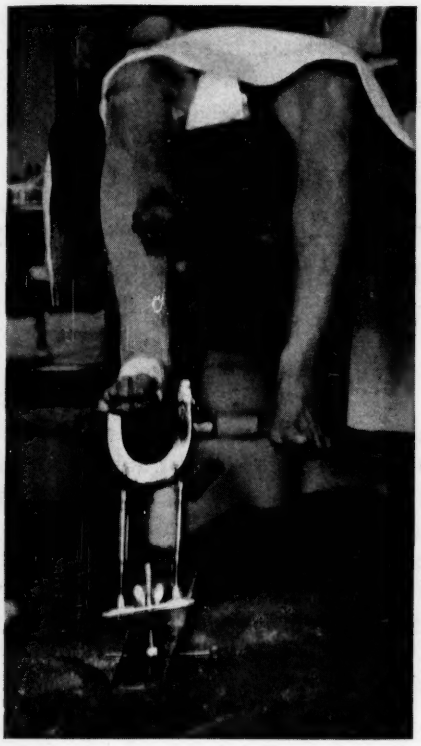

FIG. 303.—A case of compound fracture of tibia and fibula, showing the injured limb in position after reduction. Debridement has already been carried out and the wound sealed with collodion gauze.

FIG. 304.—The injured limb after reduction and with plaster applied. Second pin through tibial tubercle incorporated in plaster, fixing the upper fragment.

A large number of fractures of the lower leg, both simple and compound, have been treated by this method, with very satisfactory immediate and remote results.

Summary.—The treatment here described for fractures of the lower leg is considered to have certain advantages over the methods at present in use, for the following reasons :—

1. The apparatus is simple, not bulky either in use or in storage, and can be fixed up in a few minutes, even by the most inexperienced person.

2. An almost perfect reduction can be readily obtained, since there is no difficulty caused by the fractured leg sagging in the middle, which is very troublesome when traction is applied in the horizontal position—this being especially so in comminuted fractures.

3. The fractured leg is in the optimum position for the seated surgeon to carry out the necessary manipulations, and to apply quickly and easily a well-fitting plaster, thereby considerably reducing the time of the operation.

4. It is particularly easy to carry out radiological control with ordinary portable apparatus.

5. The flat rubber surface of the operating table is the ideal counter-traction, as opposed to the iron bar, which in spite of being suitably covered by felt may cause a pressure sore or post-operative pain.

6. The apparatus shown, although an added advantage, is not essential. A more simple structure, similar in principle, can be easily improvised in any hospital.

EXPERIMENTAL SURGERY

STUDIES IN PNEUMONECTOMY AND THE DEVELOPMENT OF A TWO-STAGE OPERATION FOR THE REMOVAL OF A WHOLE LUNG*

By F. RONALD EDWARDS, Liverpool

In the following study, an investigation has been made into the procedure of removing a whole lung and its after-effects upon the experimental animal, in order that similar changes, which occur in man after the operation of pneumonectomy, may be more fully understood. Furthermore, the possibility of performing the operation in two stages has been investigated, and a test suggested which may be performed at an early stage in the operation to decide whether the patient will successfully survive the procedure of pneumonectomy.

METHODS

Rabbits were used throughout the investigation, except for one cat in the shock experiments.

Anæsthesia.—Endotracheal differential pressure anæsthesia was employed in all operations, using a modified form of the Tiegel-Henle apparatus. Ether and oxygen were given at a pressure of 1 cm. of water, and after the pleura was opened oxygen only was administered.

The Operation of Pneumonectomy.—An incision 1½ in. long was made through the fourth intercostal space, the pleura opened, and a clamp placed across the pedicle. The ligamentum latum pulmonis was divided and the lung removed distal to the clamp. A linen thread ligature was tied proximal to the clamp, and the clamp removed. The thorax was then closed, and the muscles and skin sutured with catgut.

The Investigations.—Thirty pneumonectomies were performed with one death, 12 on the left side and 18 on the right side.

Immediate post-operative observations were made on the respiratory rate, the changes in the erythrocyte count, and the percentage of hæmoglobin therein.

The animals were killed at varying periods from six days to six months, and the changes in the anatomy of the thoracic viscera studied both macroscopically and radiologically. Sections of the remaining lung and the heart were made at different intervals after pneumonectomy.

An investigation was made into the causation of shock during the operation of pneumonectomy. The muscles, pleura, lung tissue, and hilum were stimulated mechanically and electrically, and the effect noticed upon the blood-pressure

* The substance of a Hunterian Lecture given before the Royal College of Surgeons of England, on February 8, 1939.

tracings, this being used as an index for the onset of primary shock. Variations in the pressure in the pulmonary and systemic circulation, due to the clamping of one main branch of the pulmonary artery, were studied by blood-pressure tracings taken from cannulæ inserted into the right ventricle and the carotid artery.

In a series of 21 rabbits the pulmonary artery was ligated by opening the chest as before and a silk ligature passed around the pulmonary artery and tied; 14 of these rabbits recovered. Of the deaths, 3 died from an overdose of anæsthetic, 1 died from hæmorrhage, 1 died from bronchopneumonia, and 2 died from some unknown cause within twenty-four hours. The surviving animals were examined at varying intervals from fourteen days to five months after the operation. Macroscopical and microscopical studies were made of the lungs.

The operation of pneumonectomy was performed in two stages in a series of four rabbits. The first stage consisted of ligature of the pulmonary artery; fourteen days later the chest was re-opened and the lung amputated as a second stage. The four animals survived, and similar post-operative investigations were made as in the series of one-stage pneumonectomies.

POST-PNEUMONECTOMY CHANGES

Respiration.—The normal respiratory rate in the rabbit is approximately 30 per minute. Immediately after pneumonectomy this is raised to 60–80 per minute. After removal of the right lung the post-operative rise is usually higher

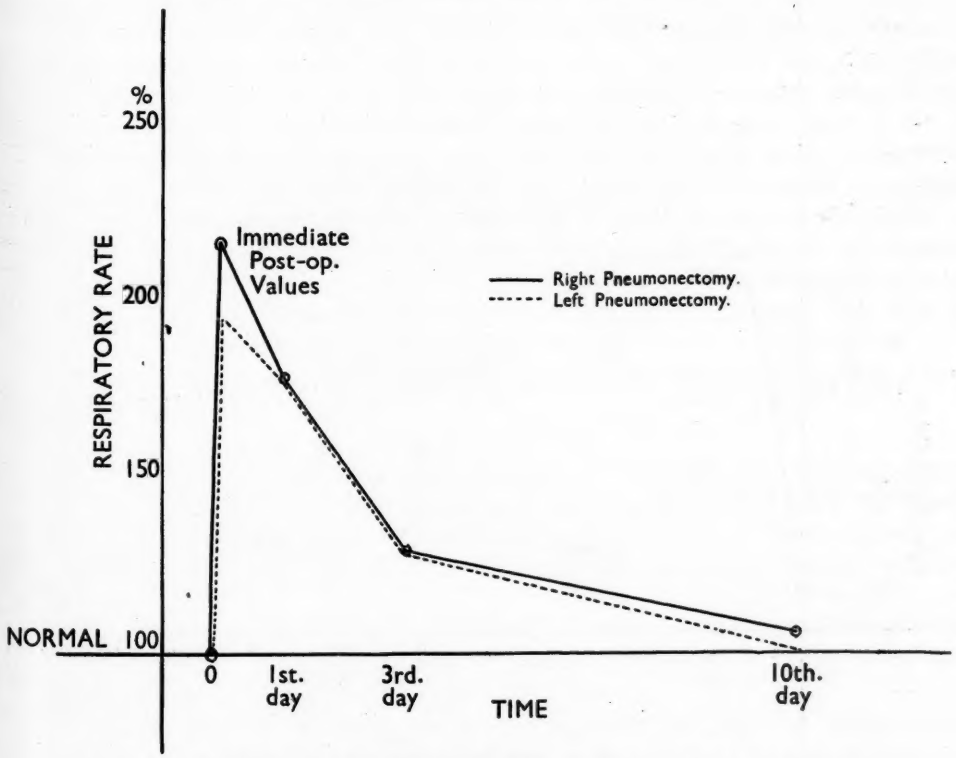

FIG. 305.—Graph showing the comparison of the percentage rise in the respiratory rate after right and left pneumonectomy.

than when the left lung is removed, and this may be accounted for by the greater size and aerating surface of the right lung.

The next day the respiratory rate is still above normal, but is falling, and is usually about 50 per minute. Three days later the figure is approaching normality, and in ten days the pre-operative value has been reached.

Fig. 305 shows the comparison between the respiratory rates after right and left pneumonectomy taken in 8 cases.

Changes in the Blood.—The blood was examined before and after pneumonectomy in 6 rabbits. An estimation of the erythrocytes and hæmoglobin was made and compared with a control series on the same diet.

The average figures were :—

	Pre-operative		Three Weeks Later	
	Red Blood-cells	Hæmoglobin	Red Blood-cells	Hæmoglobin
Pneumonectomy series	5,180,000	90 per cent	6,640,000	111 per cent
Control series (same diet, no operation)	5,060,000	90 per cent	5,160,000	92·5 per cent

In two cases a detailed blood-count was made and a graph of one is shown in *Fig.* 306.

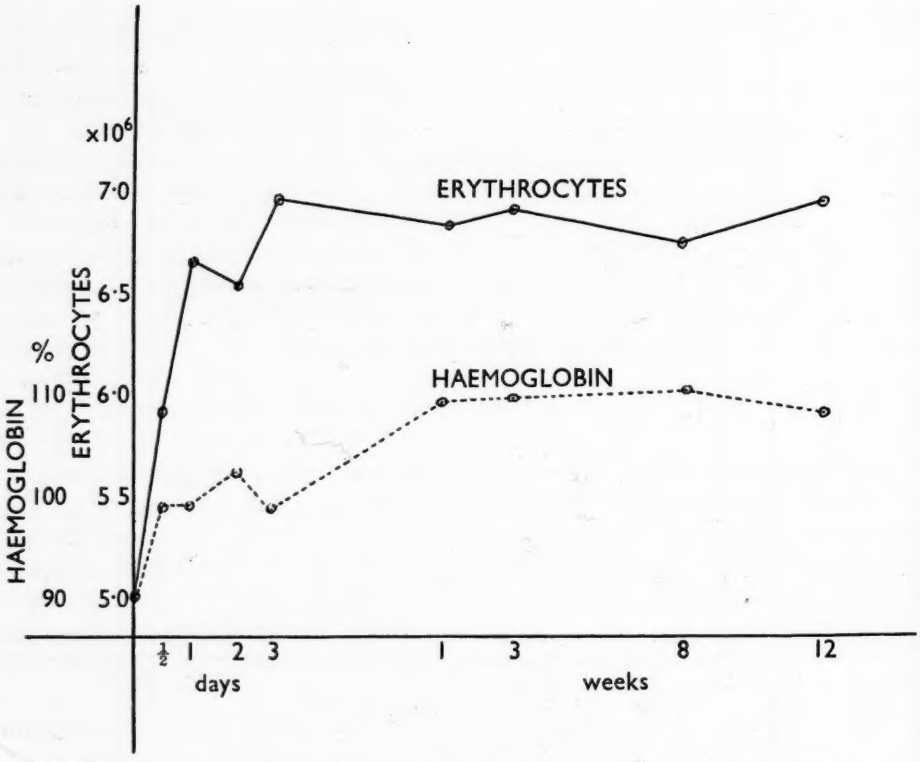

FIG. 306.—Graph showing changes in the erythrocyte and hæmoglobin count after pneumonectomy.

INTRATHORACIC READJUSTMENTS AFTER PNEUMONECTOMY

Immediately following the operation of pneumonectomy there is a small effusion into the pleural cavity of the same side. This appears within twenty-four hours, and aspiration of the chest shows it to be a clear fluid, occasionally slightly sanguineous and containing possibly a few polymorphs. In four animals in which the fluid was deliberately searched for it was found. There was only a very little and it gave rise to no apparent constitutional symptoms.

The pleural exudate clears very rapidly, and, with the absorption of the fluid and gas in the cavity, the thoracic viscera alter their anatomy and in the course of a few weeks take up an entirely new position.

The following study was made on animals six months after pneumonectomy.

The Heart and Vessels.—The heart takes no part in the readjustment, but is pushed over at the expense of the remaining lung. After removal of the left lung it moves over to the left to come into contact with the left thoracic wall; after removal of the right lung it is pushed over to the right side to come into contact with the right thoracic wall.

It rotates from an axis running through the right auricle and in line with the superior vena cava and the inferior vena cava. These two structures maintain a comparatively normal position.

After left pneumonectomy the heart rotates as well as shifts to the left, the right ventricle becoming more anterior, and the cutting of the right pulmonary veins associated with the push of the enlarging left lung enables the left auricle to take up a more anterior position.

The ventricles being quite free, except for the pericardium and the phrenico- and sterno-pericardial ligaments, which stretch easily, are able to swing in whichever direction they are pushed. The aorta and pulmonary artery, being at the base of the pendulum, are little disturbed in their normal relations.

The blind ends of the pulmonary artery and veins apparently do not thrombose, and although becoming smaller in size remain patent, and persist as diverticula off the pulmonary artery and left auricle respectively. This observation is of importance, because if thrombosis did occur, it is possible for pieces to separate off to become emboli; in the case of the pulmonary artery into the opposite lung, or in the case of the pulmonary veins into the systemic circulation. No case of embolism occurred in the thirty rabbits operated upon.

The aorta does not move very far, because of the bilateral intercostal artery attachments which serve to fix it.

The azygos veins are in normal position.

The Lung.—The remaining lung increases in size, the main increase being of the lower lobe. So much so is this that, if the lung is removed with the vessels and bronchi attached, the hilum appears to be only a quarter of the way down the inner surface of the lung instead of in the usual approximately midway position (*Fig.* 307).

The lower lobe pushes its way over to the contralateral side and fills the lower thorax on that side. The mediastinum is pushed in front of it and appears as a hernial sac in the opposite thorax (*Figs.* 308, 309).

The upper part of the lung pushes the superior and anterior mediastinum over to the opposite side, but not as completely as at the base; the remaining part of the upper thoracic cavity is filled by the thymus.

A B

FIG. 307.—Photographs of a normal lung (A), and the lung remaining after pneumonectomy (B), showing the position of the hilum in each, and demonstrating that the main enlargement of the remaining lung takes place in the lower lobe.

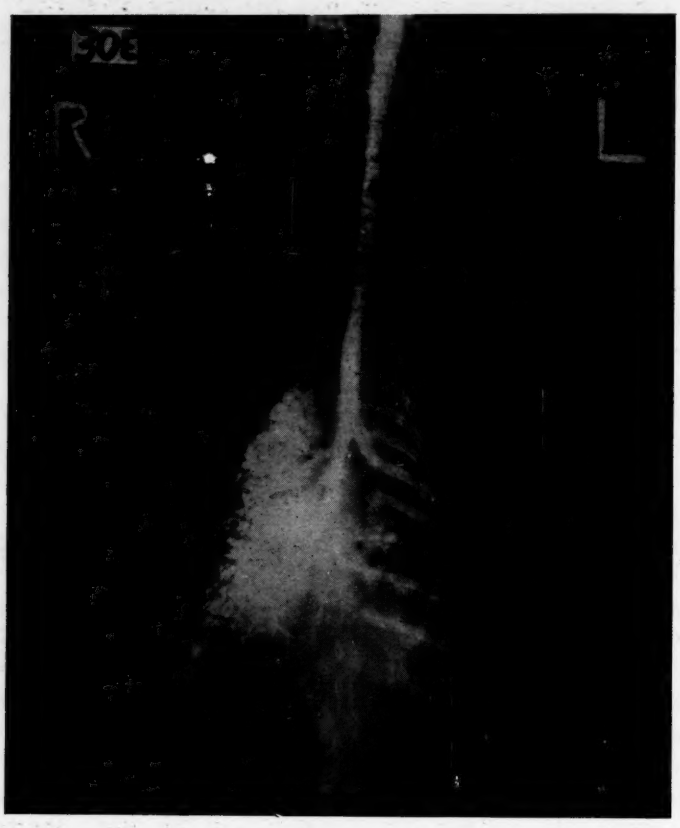

FIG. 308.—Radiograph of the chest after left pneumonectomy. The lung has been filled with a 40 per cent barium-gelatin paste. The heart has been pushed over to the left thoracic wall.

The anterior border of the lung increases in size and spreads over the anterior surface of the pericardium.

Posteriorly the lung bulges the mediastinum behind the heart and in front of the aorta towards the opposite side.

The lower lobe in passing over to the opposite side has a curious course. In the case of the removal of the left lung, the enlarging right lung passes through

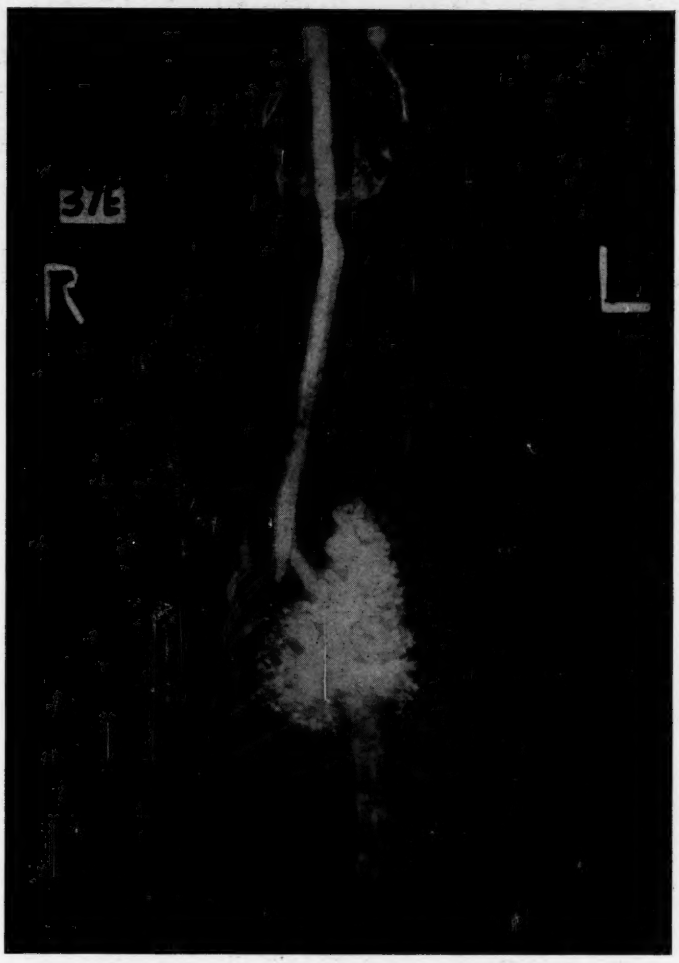

FIG. 309.—Radiograph of the chest after right pneumonectomy. The lung has been filled with 40 per cent barium-gelatin paste. Note that the heart has been pushed over to the right side of the chest.

a space between the œsophagus behind and the inferior vena cava in front. In the case of the removal of the right lung, however, the enlarging left lung passes in front of both the inferior vena cava and the œsophagus. This is a constant finding.

Examination of sections of the remaining lung tissue removed at various intervals after pneumonectomy gives the following findings: Lung tissue removed at the end of the first week showed that a very marked degree of alveolar dilatation had occurred (*Fig.* 310). During the course of the next few months the walls of the alveoli become somewhat thicker, due to the increase in the size of the capillaries

(*Fig.* 311), and this change becomes permanent by the laying down of new fibrous tissue in the form of fibrocytes which later become fibroblasts (*Fig.* 312).

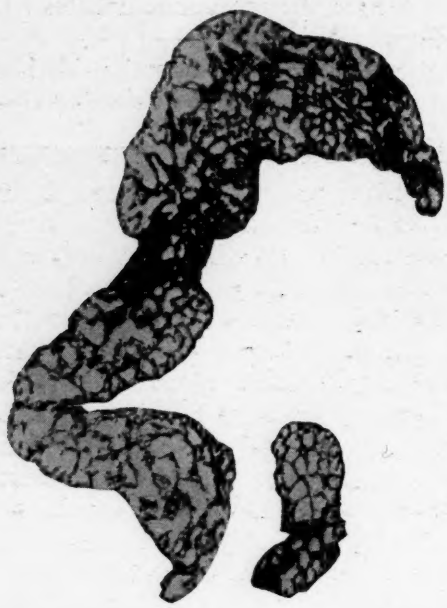

FIG. 310.—Section showing alveolar dilatation occurring in the early stages after pneumonectomy (6 days). Low-power view of a portion of the lower lobe. (× 8.)

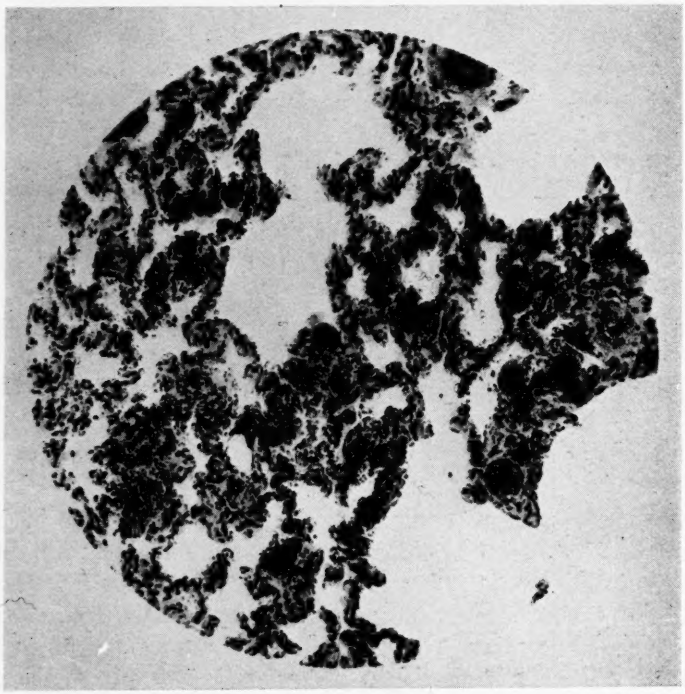

FIG. 311.—Section of the remaining lung one month after pneumonectomy. Thickening of the alveolar walls is commencing and the marked hyperæmia is shown. (× 75.)

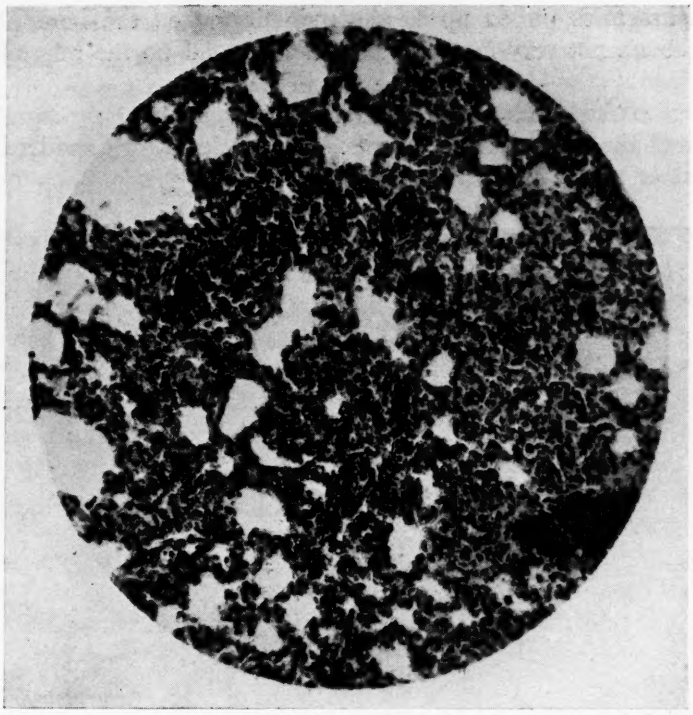

FIG. 312.—Section of the remaining lung taken five months after pneumonectomy. Note the thickening of the alveolar walls. The capillaries are larger in size and there is definite increase in the stroma. (× 75.)

The Œsophagus.—This structure, having no thoracic attachments, is deviated to the right or left to quite a marked degree by the remaining lung pushing it over to the opposite side.

The Filling of the 'Dead Space'.—The pleural space remains in all cases as a potential space. There is not true obliteration of the cavity. The mediastinal pleura comes into contact with the parietal pleura and if air is introduced a true pneumothorax is produced.

There may or may not be adhesions across the cavity. If any are present they are situated anteriorly and are almost certainly due to a little blood having escaped at the operation and having gravitated to the front when the animal resumes its normal stance. These adhesions are very fine and filmy in character and are not vascular.

The cavity is quite dry; no fluid has ever been found after the first week. The line of incision through the intercostal space is unrecognizable, and similarly the area of the original hilum is only shown by a slight puckering in the pleural endothelium. The pleura heals itself, and covers raw areas with amazing rapidity, very like the peritoneum and dura mater. If one of these chests is opened six days after operation, the pleural lining is absolutely intact and there is little evidence of any interference.

There is some slight increase in the obliquity of the ribs on the homolateral side in the endeavour to diminish the size of the thoracic cage, but this is very little. Radiographs of the chest confirm this. Scoliosis is difficult to estimate owing to the great mobility of the rabbit's spine, but there appears to be very little.

The diaphragm is pulled up to a certain degree on the homolateral side of the chest, although not very markedly, and helps to fill up the inferior part of the cavity.

There is a marked increase of fat in the thorax, particularly in relation to the pericardium and the pericardial ligaments. This helps very considerably in filling the lower part of the thoracic cavity.

OBSERVATIONS ON SHOCK IN PNEUMONECTOMY

Primary shock is considered mainly to be due to the passage of noxious stimuli to the brain, a condition which may persist even under conditions of deep anæsthesia.

Investigation into the sensitivity of the pleura has shown that both the parietal and the visceral pleura are insensitive to pain themselves. The extrapleural layer of the parietal pleura, however, possesses a very rich network of sensory nerves which is sensitive to stimuli. These points are best made out by means of a thoracoscope inserted through a cannula in the chest wall, a preliminary pneumothorax having been induced. Through a second cannula any form of stimulating apparatus may be introduced.

The following observations have been made during the operation of thoracoplasty and division of adhesions in cases of pulmonary tuberculosis. The operation is performed under local anæsthesia, hence the patient is conscious and can give a positive answer as to the results of stimulation. Forms of stimulation used were a fine point, a coarse point, heat, and a pair of forceps to grip the pleura and produce traction upon it.

The parietal pleura is insensitive to light touch with a fine point, but as soon as the point penetrates into the extrapleural tissues pain is felt. Heavy pressure upon the pleura and the close proximity of heat is felt by transmission through to the extrapleural layer. Dragging on the pleura produces a painful stimulus.

The visceral pleura appears, however, to be completely insensitive to the stimuli of pain, heat, and dragging.

It appears that the only structures in the lungs that give rise to pain stimuli are the blood-vessels, spasm of which, as occurs when a pulmonary embolism becomes lodged, producing a diffuse pain in the chest. Other pulmonary conditions, provided that the extrapleural layer of the parietal pleura is not involved, are painless.

The bronchus does not transmit pain stimuli below the bifurcation of the trachea, as can be shown both clinically and by passing a bronchoscope. Gross deviation of a bronchus by pressure on a bronchoscope, however, will produce pain by stimulation of the nerve-plexuses in the mediastinum.

In the experimental animal, after the lung has been amputated, rotation of the clamp still remaining on the hilum produces an interesting effect upon the blood-pressure. If the clamp is rotated posteriorly, i.e., stretching the anterior surface of the hilum, no effect is noticed. If, however, the clamp is rotated anteriorly, even through only 20°, then there is a sharp fall in the blood-pressure, which persists at a low level until the rotation is relieved. A similar effect is produced by traction upon the hilum (*Figs.* 313, 314). It was at first thought that this was a reflex action produced from stretching the posterior pulmonary nerve-plexus, but it has now been found to be due to the distortion of the main pulmonary artery at its bifurcation. This distortion, which is very easily produced, causes

obstruction, the right ventricle dilates markedly, the blood-flow through the lungs to the systemic circulation diminishes, and consequently the blood-pressure falls. This obstruction to the pulmonary circulation is associated with a marked deepening of the animal's respirations, and an irregularity both in depth and time. Jactitation and convulsive movements of the whole body occur, particularly if the anæsthesia is fairly light.

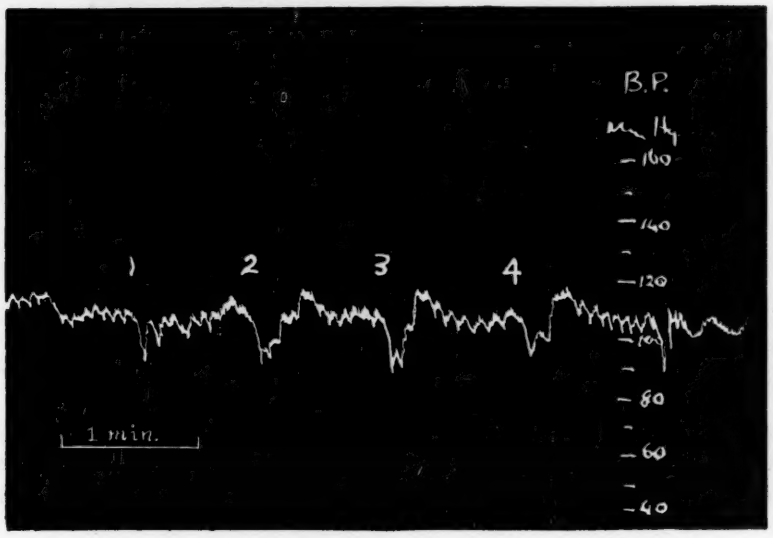

FIG. 313.—Tracing showing the effect of traction on the lung hilum on the systemic blood-pressure in the cat.

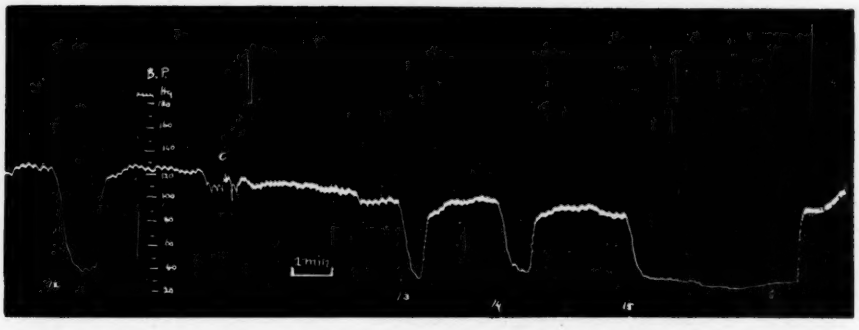

FIG. 314.—Similar tracing to *Fig.* 313 after the injection of novocain into the lung hilum. Demonstrating that fall in the blood-pressure is due to mechanical means and is not reflex in origin.

Experiments on the cadaver in man have shown that this distortion of the pulmonary artery can be very easily produced by minor rotations of the hilum.

If this obstruction is maintained the animal rapidly deteriorates in condition.

THE PULMONARY CIRCULATION AFTER PNEUMONECTOMY

One of the effects of pneumonectomy is instantaneously to cut down the pulmonary vascular field by half.

The result of this is that the systolic pressure in the pulmonary artery goes up by 50 per cent from 20 mm. to 30 mm. Hg (*Fig.* 315). It persists at this

level for about half an hour and then starts to fall as the vessels in the opposite lung begin to dilate. Twenty-four hours after pneumonectomy the pressure appears to have fallen to normal again, although there is some difficulty in obtaining accurate readings when dealing with such small pressures.

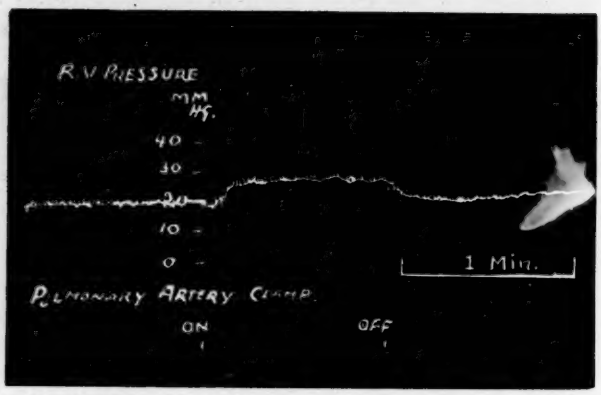

FIG. 315.—Tracing of the pressure in the main pulmonary artery. A rise of 50 per cent is obtained on clamping the lung hilum, and the blood-pressure falls to normal again immediately on loosening the clamp.

Although the pulmonary pressure rises by approximately 50 per cent, there is no slowing of the heart rate, and apparently there is no reflex mechanism on this side of the heart similar to the cardio-aortic nerves on the left side of the heart, which slows the heart rate in response to raised aortic pressure.

The systemic circulation also suffers a slight fall in pressure, usually 10–15 mm. Hg, when one branch of the pulmonary artery is clamped (*Fig.* 316). This, however, recovers rapidly.

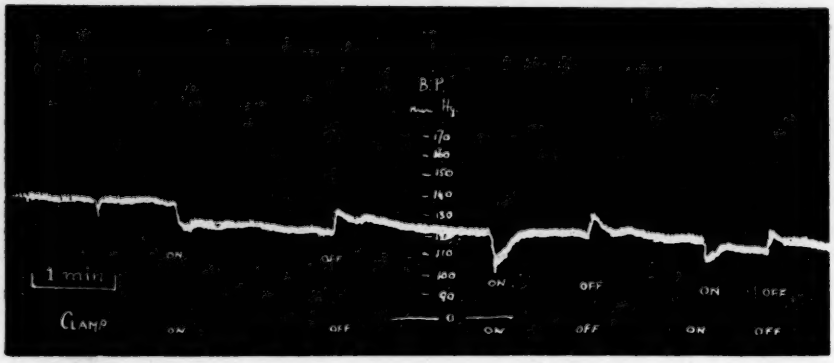

FIG. 316.—Tracing showing transient fall in the systemic blood-pressure following clamping of the hilum.

Observation of the pulmonary artery and veins of the remaining lung show that these structures dilate to practically double their normal size in the course of a few minutes, and they remain in this state for the rest of the animal's existence.

Dissection of the pulmonary artery six months after pneumonectomy shows the remaining main branch of the pulmonary artery to be as big as the main pulmonary artery itself.

Electrocardiographic studies of the rabbit's heart have been made before and after ligature of the pulmonary artery, but no information of definite value could be obtained.

Sections of the wall of the right ventricle taken six months after operation, compared with the normal ventricular wall, suggest that a considerable degree of hypertrophy has taken place, and certainly on macroscopical examination of the right ventricle it appears to be larger and thicker than normal.

THE EFFECTS OF LIGATURE OF THE PULMONARY ARTERY

The lung, the pulmonary artery of which had been tied, was about half the normal size and very firm. It appeared to be much paler in colour than normal.

There were numerous adhesions to the chest wall, mediastinum, pericardium, and diaphragm, which were extraordinarily vascular.

The mediastinum was pulled over to the affected side, and the lung on the opposite side was enlarged, although not as much as occurred in pneumonectomy.

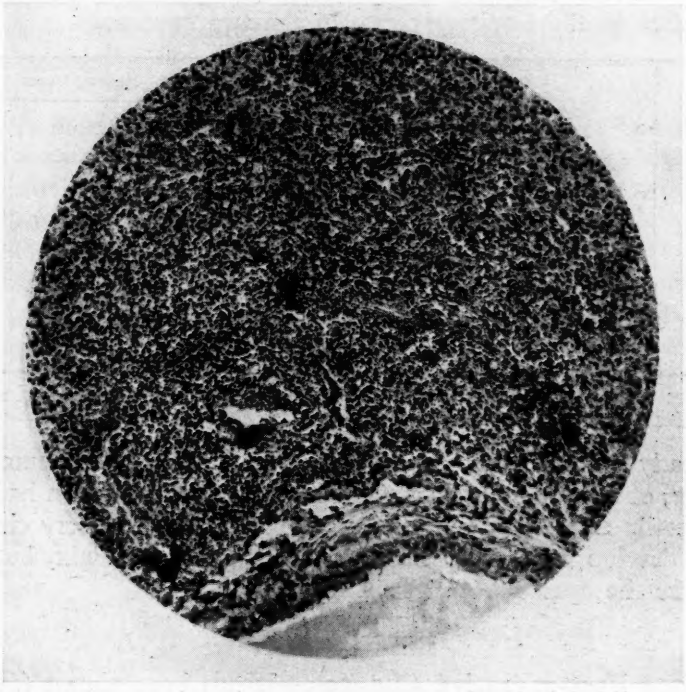

FIG. 317.—Section of the lung after ligature of the pulmonary artery. There is collapse of the alveoli, but the lung still remains viable. The blood in the capillaries is coming from the bronchial circulation. Fibrosis is occurring. (× 75.)

The blood-vessels were, however, increased to the same degree of size as is seen after removal of a lung.

The changes in the thoracic anatomy corresponded to a minor degree with those seen after pneumonectomy.

Section of the lung showed a complete collapse of all the alveoli, with a marked degree of fibrosis occurring in the parenchyma (*Fig.* 317). The vascularity of the

lung was much diminished, but there was still some blood flowing through it, as shown by the fresh red blood-cells in the vessels. This comes from the hypertrophied bronchial vascular system, which can easily be seen in these cases.

These lungs were living on the bronchial circulation only, and an accessory supply obtained from the surrounding parietes and viscera.

We may conclude from these experiments that, providing the bronchial circulation is intact, the lung will still live at a minimal rate after ligature of a main branch of a pulmonary artery.

EXPERIMENTAL TWO-STAGE PNEUMONECTOMY

The preliminary ligature of the pulmonary artery was performed satisfactorily in this series. On opening the chest fourteen days later there were numerous adhesions that could be easily separated with the finger. There was a little bleeding from some of them, but their vascularity was as yet small. The lung was quite firm, and pneumonectomy was very easy.

The post-operative rise in the respiratory rate was measured and found to be much lower than that seen in simple pneumonectomy. The following table gives the relative rises in the respiratory rate in the two operations.

Animal No.	Side	Percentage Rise in Respirations			
		Pre-operative	Immediate Post-operative	24 Hours	3 Days
71E	L	100	160 (193)	125 (173)	100 (127)
72E	L	100	160	125	112
73E	R	100	166 (216)	133 (175)	100 (127)
74E	R	100	175	133	110

The figures in brackets refer to the percentage rise found in the series of one-stage pneumonectomies (left and right).

This greatly reduced reaction following the operation of pneumonectomy as a second stage, effectively demonstrates that vascular compensation had taken place quite satisfactorily as a result of the first operation. An accessory circulation was beginning to develop from the parietes at the end of a fortnight, but not to any degree to make the operation a difficult one.

DISCUSSION

Immediate Post-operative Changes.—It has been shown (*Fig.* 305) that pneumonectomy on the right side produces a greater post-operative rise in the rate of respiration than on the left side, but that in ten days' time in both cases normality has been reached again. This is due to two factors: firstly, the expansion of the remaining lung tissue; and secondly, the changes in the blood.

Andrus[1] (1923) measured the total lung volume in dogs after pneumonectomy. Immediately after operation this showed a diminution of 42 per cent. The volume begins to increase at once, however, and in twenty-four hours has risen by 8 per cent. It reaches the pre-operative level in from twenty to twenty-six days after operation.

Heuer and Andrus[2] (1922) found also in dogs that the alveolar carbon dioxide rises until the eleventh day and then gradually falls. The alveolar oxygen falls at a rate comparable to the carbon dioxide until a minimum is reached on the eleventh day, when it gradually returns to normal. These two findings are associated with a temporary rise in the carbon-dioxide content and a marked rise in the percentage of oxygen unsaturation.

It has been shown, however, that there is an almost immediate rise in the number of red blood-corpuscles and hæmoglobin in the blood, which acts as a compensatory mechanism and accounts for the rapid recovery from the dyspnœa. In fact after three days the animals are perfectly lively and running about their cages.

Within twenty-four hours the number of red cells had increased by 25 per cent and the hæmoglobin by 10–15 per cent, and a maximum is reached by the third day. This raised blood-count and hæmoglobin value persisted for the rest of the animal's life.

It is the stimulation of the anoxic blood upon the bone-marrow that produces this rapid formation and passage into the circulation of the red blood-cells. At the same time the anoxæmia produces marked contraction of the spleen which throws into the circulation further red blood-cells, and Barcroft[3] has shown that these cells have a higher hæmoglobin content than normal.

Jacobaeus, Frenckner, and Bjorkmann[4] (1932) have shown by bronchospirometric experiments that in accordance with the anatomical fact that the right lung makes up 54 per cent, and the left lung 46 per cent, of the aggregate volume of both lungs, exactly the same ratio is found to apply to their function. *Fig.* 305 demonstrates this fact, and shows that pneumonectomy on the right side is a more serious procedure than pneumonectomy on the left side.

The small amount of fluid that is found in the pleural cavity after pneumonectomy is a fairly constant factor after any intrapleural manipulation, and in fact, after any surgical procedure performed inside an endothelially lined cavity.

Heuer and Dunn[5] (1920) failed to find it in any of their series of cases and concluded that if it was present then it was due to infection. This is doubted, as in no case has pus been found or thickening of the pleura noticed at post-mortem examination. Schepelmann[13] (1913) states that in dogs, the large cavity left after removal of the lung becomes filled first with a serous transudate which only disappears with obliteration of the cavity.

Kawamura[6] (1914) states that contrary to the experience of Sauerbruch, Robinson, and Haecker[7, 8] (1910), he found no fluid in the pleural cavity.

A small amount of blood, even a few drops, in the pleural cavity in association with a pneumothorax, is almost invariably followed by a pleural transudation which is not great in amount.

Pleural cavities however, even in human beings, vary in their reaction to trauma, pneumothorax, and the presence of blood, and it may be that the pleura of the dog is less sensitive than that of the rabbit. Enough is not yet known about the production of exudates and transudates in the pleural cavity to be dogmatic on this point.

The Expansion of the Remaining Lung.—It has been shown in the radiographic and post-mortem examination of the animals that there is a marked increase in the size of the remaining lung after pneumonectomy (*see Figs.* 308, 309). This increase in size may be due to three factors.

1. There may be an increase in the size of the air spaces of the lung, without corresponding increase in the structure, i.e., *alveolar dilatation.*

2. There may be an increase in the size of the functional respiratory units, without actual increase in number, i.e., *hypertrophy.*

3. There may be actual new growth of lung tissue, i.e., *hyperplasia.*

The part that these three processes play has been a subject for much discussion. The three terms used above have been indiscriminately applied in the literature, without consideration of their true meaning. 'Compensatory emphysema' is a phrase used frequently, but as Behrend[9] (1937) points out, if emphysema occurs it is in no way an asset to the function of the lung—in fact the lung is less efficient in emphysematous areas than in the normal lung, and in no sense can it be compensatory as far as the function of the lung is concerned.

Alveolar dilatation can easily be seen microscopically, but true hypertrophy and true hyperplasia are extremely difficult to assess. Hellin[10] (1906) said that the findings were not clear in his work; hypertrophy seemed to be present, possibly hyperplasia, but emphysema certainly was not present. Quinby and Morse[11] (1911) deny the existence of emphysema. Friedrich[12] (1908), Schepelmann,[13] (1913), and Kawamura[6] (1914), however, were of the opinion that emphysema was present. The latter author also saw hypertrophy, but could not be sure of hyperplasia. Möllgaard[14] (1909) considered the alveolar spaces to be dilated without atrophy of the partitioning walls. Behrend[9] (1937) considers emphysema, hypertrophy, and hyperplasia to be absent, and that the increase in size is due to fibrocytic proliferation in the walls of the alveoli. Morrison[15] (1926) notes that emphysema is present, and describes the thickening of the alveolar walls, but does not comment on lung hypertrophy or hyperplasia.

Certainly, on macroscopic examination of the lung, there is little evidence to suggest that gross emphysema is present. It looks normal except, perhaps, for the edges of the lobes.

Hyperplasia is a rare condition to occur in mammals once the growth period has passed. True hypertrophy is commoner, however. Many of the organs have an enormous functional reserve which is called upon in time of stress, and if this stress is prolonged, as occurs when a portion of an organ is permanently removed, then true hypertrophy will take place. Mann[16] (1921) has shown by his experiments the great reserve of the liver; similarly Richards and Schmidt[17] (1924) have shown the great reserve of the kidney. Higgins and Anderson[18] have shown that if three-quarters of the whole liver is removed it will have regained its normal size within four weeks by reason of the rapid increase in size and number of hepatic cells in the lobule. The lobules, however, do not increase in number. Furthermore, all this process is dependent on an adequate blood-supply, for if an Eck fistula is performed the liver does not hypertrophy. The answer to the problem of lung regeneration will probably be found along these lines.

After pneumonectomy, the condition in the remaining lung is comparable to a state of continuous exercise. The tidal air passes into one lung, and the total blood-flow passes through this one lung. In fact, this one lung has a permanent double amount of work to perform. From the evidence at our disposal, it is very probable that the following series of events takes place in the opposite lung after pneumonectomy. Firstly, a certain degree of alveolar dilatation (*see Fig.* 310) will take place almost immediately, due to an attempt on the part of the remaining lung

to fill the thoracic cavity following the absorption of the air and the fluid on the opposite side. New capillaries will open up (*see Fig.* 311) and many of the alveoli which had been working previously at minimal capacity commence working maximally. As a result of the increased blood-supply in the walls absorption of oxygen is increased and consequently the alveoli can still enlarge to a certain extent and remain efficient as aerating units, and in fact, if the hyperæmia is marked, can conceivably be more efficient than before. This is contrary to the state of affairs that occurs in the simple emphysema secondary to bronchial asthma and chronic bronchitis, in which the blood-supply to the alveolus is not increased. The walls of the alveoli become somewhat thicker due to the increase in the size of the capillaries, and this change becomes permanent by the laying down of new fibrous tissue as is shown in *Fig.* 312. If alveolar dilatation occurred without the formation of new tissue, then the lung, with the blood removed, should weigh the same as a normal lung. If, however, hypertrophy takes place as well, then the lung in an exsanguinated condition should weigh heavier than normal.

This is exactly what does occur, as the following experiment demonstrates. Pneumonectomy was performed upon four rabbits. A right pneumonectomy was done in each case, as the remaining left lung is the smaller and would undergo the greatest degree of hypertrophy if this was to take place. Three months later they were killed. Before the heart had stopped beating the thorax was opened and a cannula inserted into the pulmonary artery via the right ventricle. The left auricle was incised. The pulmonary vascular system was washed through for a period of five minutes with distilled water, by which time the efflux from the left auricle was clear. The lung was then removed at the hilum.

A second series of normal animals of exactly the same weight were subjected to the same procedure, and both lungs removed from each.

All the lungs were then placed in a drying oven, heated to 100° C., and desiccated for eighteen hours, by which time they were completely dry. They were then weighed and the following results obtained.

All animals weighed approximately 2 kg.

Pneumonectomy (Right) Series

Animal No.	Weight of Left Lung Desiccated
85E	1·49 g.
85E	1·59 g.
93E	1·40 g.
94E	1·40 g.

Control Series

Animal No.	Weight of Right Lung Desiccated	Weight of Left Lung Desiccated	Weight of Both Lungs Desiccated
1LC	0·86 g.	0·58 g.	1·44 g.
2LC	0·92 g.	0·62 g.	1·54 g.
3LC	0·96 g.	0·54 g.	1·50 g.
4LC	0·89 g.	0·62 g.	1·51 g.

All these lungs were dealt with under the same conditions, and it is seen that after three months the remaining lung weighs very nearly as much as the original two lungs together. The left lung had increased its weight by approximately two-and-a-half times the original weight.

This is due to two factors, the laying down of new tissue and the increase in the size and therefore the weight of the blood-vessels. This last factor cannot

be eliminated, but in all probability does not account for a very high percentage of the increase.

Further evidence that hypertrophy occurs in the lungs is given by the bronchial arteries. Examination of these structures in the rabbit shows a minute artery running to each bronchus from the aorta and being distributed along it, which may be duplicated on one or both sides of the chest. When pneumonectomy is performed, the bronchial artery or arteries to the remaining lung undergo a very considerable increase in size. It is known that the bronchial artery is nutritional to the lung structure, and the increase in size suggests that there is an increase in this structure, but of course does not differentiate between hypertrophy and hyperplasia.

No evidence can be found, however, to suggest that true hyperplasia takes place in the adult lung, though it is more than possible that actual new formation of lung tissue takes place in the lung of the growing animal or child, as has been shown by the work of Haasler[19] (1892), Hilber[20] (1934), Bremer[21] (1937), and Longacre, Carter, and Quill[22] (1937).

There is thus no reason to suggest that the lung responds to partial removal in any different manner than does any other organ in the body subjected to the same procedure.

The Lung with the Pulmonary Artery Ligated.—The observations made on the condition of the lung after the pulmonary artery had been ligated, agrees with the work of Bruns and Sauerbruch[23] (1911) and Schlaepfer.[24] The bronchial artery is well able to maintain the nutrition of the lung in the absence of the pulmonary circulation. There is, however, a great tendency for an accessory circulation to the lung to be developed from the surrounding structures. This occurs by the formation of adhesions of great vascularity. These do not develop, however, until a month or two after the pulmonary artery has been tied.

Pneumonectomy in Two Stages.—Ligature of the pulmonary artery allows the respiratory and vascular changes associated with pneumonectomy to occur without the gross displacements of the thoracic anatomy.

At the second stage when the lung is amputated, the post-operative dyspnœa is much diminished in amount, and shorter in time, as shown by the table of comparative rise in respiratory rates.

Amputation of the lung is unassociated with any rise in the pressure in the pulmonary arterial system, and there is no dilatation of the right ventricle.

CLINICAL APPLICATIONS OF EXPERIMENTAL OBSERVATIONS IN TOTAL PNEUMONECTOMY

The success of the operation of pneumonectomy as performed in man, depends upon two factors :—

1. The ability of the contralateral lung to take over the function of the two lungs.
2. The ability of the pulmonary vascular system in the contralateral lung to adapt itself to a permanently increased flow.

The operation of dissection pneumonectomy is a long one and all methods for the avoidance of shock must be utilized.

Before the operation of pneumonectomy is embarked upon, a very complete investigation of the vascular system should be performed. Evidence of arterio-sclerosis suggests that a similar condition in the pulmonary vessels may be found,

and that dilatation in these structures may be slow, with a coincident back-pressure upon the right ventricle after operation.

Anæsthesia and Shock.—Modern methods of general anæsthesia have all given satisfaction in this operation. The fact that the operation can be successfully performed under unilateral spinal anæsthesia has demonstrated that positive pressure is not necessary. 'Anoci-association', however, has been shown to diminish shock, and the procedure of spreading of the ribs produces much less disturbance to the patient if a preliminary intercostal nerve-block has been performed.

It has been shown that the parietal and visceral pleura and the lung itself do not give painful stimuli to touch and normal manipulations and thus can be eliminated as shock-producing factors. Shock produced at the hilum, however, deserves discussion.

Morrison[15] (1926) made the observation that pneumonectomy in rabbits was not possible without previous section or blocking of the vagus nerve on that side. In his experiments on animals with normal vagi, he found that on attempting to perform a pneumonectomy, as soon as the hilum was clamped the respirations became irregular and ceased in full inspiration. He drew the conclusion that powerful nervous stimuli from the grossly traumatized pulmonary root interfered with the reflex of respiration via the anterior and posterior plexuses. If, however, the vagus was divided this did not occur. This phenomenon has not been seen in this series of thirty experimental pneumonectomies, and O'Shaughnessy[25] (1936) fails to notice this effect in his study of the vagus in the thorax. The administration of atropine and section of the vagus both homolaterally and bilaterally made no obvious difference to the animals in this respect. There appears to be no necessity therefore to block the vagus nerve before clamping the hilum.

Mason[26] (1936) has recorded jactitation and convulsive movements of the body in a pneumonectomy patient and a lobectomy patient during manipulations at the hilum. They were particularly noticeable when tightening the mass ligatures, which procedure usually necessitates some pulling on the hilum. Quoting Mason's words: "During manipulation in the interlobar fissure at the hilus and whenever the mass ligatures were tightened there were curious bodily jerks, which appeared to be violent respiratory movements: in addition and simultaneously, the auricles were seen to distend the pericardium, whilst the aorta apparently ceased beating. These disturbances can be reproduced with comparative ease in the cat by electrical stimulation applied deep in the interlobar fissure. . . . This suggests the possibility of these phenomena being reflexes of a nervous, probably vagal, nature . . ." Mason was able to get this phenomenon to recur fifteen to twenty times in one patient.

Attempts have been made to reproduce these results of Mason's. They can be produced quite easily, but only by a current of considerable power. This probably spreads into the mediastinum and the cardiac nodes and accounts for his findings. Stimulation of the interlobar fissure and of the hilar region by a current of low power, but strong enough to excite any reflex that might be present, produces no effect upon the heart or blood-pressure; there may be, however, some change in the respiratory rhythm.

The fact that distortion of the pulmonary artery can be so easily produced, and the effects thereof so resembling the curious symptoms described as occurring

during manipulations at the hilum of the lung, suggests that these symptoms are more mechanical in origin than reflex, and are in fact produced in man by partial obstruction of the main pulmonary artery.

Traction or rotation of the hilum should, therefore, be minimal.

The question of whether novocain should be put in the hilum before clamping, ligaturing, or dissecting it is important. The vagus has been eliminated as a potential cause of shock. The only structures that can be found to produce pain in the lung are the vessels, which are supplied by the sympathetic nervous system. We know that clamping, pulling, and ligaturing these vessels is excessively painful. For this reason a local anæsthetic at the hilum is of value. It is necessary to wait a short time until this is absorbed by the nerves to or on the vessel walls, but a short halt at this stage of a lobectomy or pneumonectomy is of great benefit to the patient. If, however, there is difficulty in putting this local anæsthetic into the hilum, as may be the case because of adhesions or thickening of the hilum, it is probably better to omit this adjunct rather than run the risk of puncturing a pulmonary vein and thereby making the operation very much more difficult.

Shock due to loss of blood should not occur if the procedure of pneumonectomy is performed in anatomical order.

Time may be consumed, and a considerable loss of blood take place, during the cutting of adhesions, but the use of diathermy greatly facilitates this manœuvre, and the division is hæmostatic.

Loss of blood must be rectified by appropriate means. Blood transfusions should, however, be given with extreme care as the right ventricle is already labouring under a heavy load and any increase in blood-volume may have fatal results; a blood-drip of the Marriott type is the best apparatus to use. Intravenous salines are for a similar reason better withheld, and saline administered per rectum only.

Closure of the Bronchial Stump.—Leakage from the bronchial stump is one of the most potent causes of death after pneumonectomy, due to infection or tension pneumothorax.

Owing to the plates of cartilage in its wall the main bronchus has always been a difficult structure to occlude. But this difficulty seems now to be less apparent, judging by the successful results obtained in man by utilizing simple forms of closure.

In the experimental field, many methods have been suggested, but a number of these are contrary to the principles of modern operative surgery.

Methods that involve opening the bronchus or transfixing with ligatures—Friedrich[12] (1908), Halsted[27] (1909), and Henschen[28] (1914)—are almost certain to infect the pleural cavity. The use of grafts of lung tissue (Garré[29]) or fascia lata—Giertz[30] (1914)—appear to be unnecessary, as the suture of the pleura over the bronchus will supply this need. Metal rings—Heuer and Dunn[5] (1920)—will nearly always cause ulceration of the bronchus, and preliminary stenosis of the bronchus with 30 per cent silver nitrate solution—Adams and Livingstone[31] (1932)—takes a considerable time to be effective, and time is important, particularly in carcinoma patients.

Simple ligation of the bronchus after crushing—Robinson and Sauerbruch[7] (1910), Heuer and Dunn[5] (1920)—or double ligation—Thomas, Behrend, and Mann[32] (1937)—appear to have given the best results, and conform to modern surgical technique.

In the present series of thirty pneumonectomies the crushed bronchus had a single ligature of linen thread firmly tied. In the course of a few days the stump became covered with fibrous tissue and the pleural endothelium had grown over it. No case of leakage had occurred.

One point, however, must be made clear. The bronchus of a rabbit has less bacterial flora than the bronchus of man, and furthermore we are here dealing with normal lungs. But the criticisms of the methods advocated hold good for the human bronchus as well as for the rabbit's bronchus, and the collected evidence suggests that simple ligation, after crushing, with suture of the pleura over the stump will give the most satisfactory results in man.

Filling in of the 'Dead Space'.—In the young child, the displacement of the lung, the heart, the chest wall, and the diaphragm, rendered possible by the considerable motility of structures at this age, may combine to produce such a complete obliteration of the cavity that it may be reduced to a potential space as in the experimental animal.

In the child, too, hypertrophy of the lung tissue is easily produced, and in fact hyperplasia may take place to a very considerable degree. The result of this is that at the end of six to nine months, provided that adequate pulmonary exercises have been undertaken, the respiratory function of the child should be practically normal again.

In the adult, however, all these structures are more rigid, and the expansion of the lung, taking place by hypertrophy only, may not be enough to close the cavity. Then ancillary methods of collapse must be considered, such as phrenicectomy or thoracoplasty. The possibility of maintaining a permanent pneumothorax on the pneumonectomized side is one that has not been fully investigated as yet.

Phrenicectomy is probably better left until the necessity for this procedure is apparent. Routine crushing of the phrenic nerve at the time of the operation should not be done. The diaphragm, even on the operated side, helps very considerably in the respiration of the remaining lung, in particular immediately post-operatively, when every means for producing expansion of the thoracic cavity should be maintained. Furthermore, it helps to maintain the negative pressure in the homolateral side and assists in the enlargement of the remaining lung.

One-Stage or Two-Stage Pneumonectomy.—In the operation of pneumonectomy in the child there is every possibility of the pulmonary vessels in the remaining lung dilating satisfactorily and hence a very rapid, if not immediate, compensation taking place for the altered pressures. However, in men of the carcinoma age a certain degree of sclerosis is usually present and the compensation will take place more slowly, or may not do so at all. During this time the right ventricle is working at a constant disadvantage, and if it has little reserve, cardiac failure is likely to supervene.

The operation of one-stage pneumonectomy will probably be successful in all young patients and many older patients, but it is particularly in that group of patients in which the pulmonary circulation cannot be deviated to the opposite lung by a preliminary pneumothorax, and in the group where early circulatory changes are already manifest, that grave circulatory symptoms may supervene as a result of the occlusion of one main branch of the pulmonary artery and the superimposed effects of the removal of the lung.

It is with the view of minimizing these dangers that the two-stage operation, with ligature of the pulmonary artery as a first stage, is presented.

The indication for this type of operation is as follows: If the collapse of the lung is complete, then a one-stage operation will in all probability be satisfactory. If the collapse is only partial or absent, then the operation can be proceeded with as far as the dissection of the pulmonary artery. A temporary ligature is placed around the vessel or the artery digitally compressed, and the right ventricle watched. The blood-pressure and the pulse-rate is taken continuously at this period. If there is gross evidence of cardiac or circulatory disturbance, then it would be wiser to abandon the operation. If the disturbance is only slight then the ligature may be tied and the amputation can safely be left until a later date. If no disturbance is produced, or is only very temporary, then the pneumonectomy may be completed in one stage.

Compression of the pulmonary artery is thus used as a test to judge whether the patient's circulatory system will stand pneumonectomy.

Since writing this paper I have learnt that Rienhoff[33] has carried out this procedure on a number of cases of pneumonectomy in man, and his results and observations will shortly be recorded in the medical press.

CONCLUSIONS

In pneumonectomy, primary shock is produced during the operation by noxious stimuli from the parietes, the extrapleural tissues, and the pulmonary blood-vessels. All other structures are insensitive. The presence of shock-producing hilar reflexes has been doubted, and it has been demonstrated that these are probably produced by mechanical obstruction at the bifurcation of the main pulmonary artery.

There is enlargement of the remaining lung, and a swinging over of the heart and the œsophagus has been shown. The pulmonary arterial pressure rises and there is a temporary fall in the systemic blood-pressure after pneumonectomy.

There is an immediate rise in the erythrocytes of 25 per cent, and a similar rise in the hæmoglobin after pneumonectomy.

The filling of the space left behind when the lung is removed has been shown to be due to the enlargement of the remaining lung and to an increase of fat in the thorax. Collapse of the chest wall and the rise of the diaphragm play only a minor part in this obliteration.

The causation of the enlargement of the remaining lung has been found to be due in the first instance to alveolar dilatation, but later there is a true hypertrophy of the lung. Hyperplasia has not been demonstrated in the adult, but is probably present in the child.

The lung can remain viable under favourable circumstances after ligature of the pulmonary artery. It lives satisfactorily on its blood-supply from the bronchial arteries. There is, however, complete atelectasis.

Finally, it has been shown that the operation of pneumonectomy can be performed in two stages, and that the crucial point of the operation is the ligature of the pulmonary artery. The circulatory effects produced by this procedure give indications whether: (*a*) The operation can proceed as a one-stage pneumonectomy; (*b*) The operation should be performed in two stages, the first stage being

ligature of the pulmonary artery only, and the second stage amputation of the lung at a later date; or (*c*) The operation should be abandoned.

This study has been performed in the Experimental Laboratories of the Department of Surgery of the University of Liverpool under the direction of Sir Robert Kelly, to whom my gratitude is due for his continued encouragement and much helpful advice. My grateful thanks are due to Mr. H. Morriston Davies, who has placed his great experience in this branch of surgery at my disposal, and whose criticism of this work has been of the greatest value. I am greatly indebted to Professor John Beattie, of the Royal College of Surgeons of England, for his help in the compilation of this paper, and to Dr. E. L. Rubin, of the Department of Radiology of the Liverpool Royal Infirmary, for the radiographs.

Finally must I thank Mr. Harold Nevin, whose technical assistance and superintendence of the care of the animals has made this investigation possible.

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SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF OBSTRUCTIVE JAUNDICE CURED BY THE CONSTRUCTION OF A NEW BILE-DUCT

By CECIL P. G. WAKELEY, London

Cases of injury to the common bile-duct during operations on the biliary system are by no means uncommon, and the literature dealing with this subject is considerable. Reconstruction of a damaged common bile-duct by Walton's method probably gives the best results, but there is no consensus of opinion as to what is the best procedure to adopt in cases in which the common duct is obliterated and no part of it or the common hepatic duct can be found, and therefore no anastomosis between the biliary system and the gut can be performed. The attempts at hepatico-enterostomy have failed to give good results because,

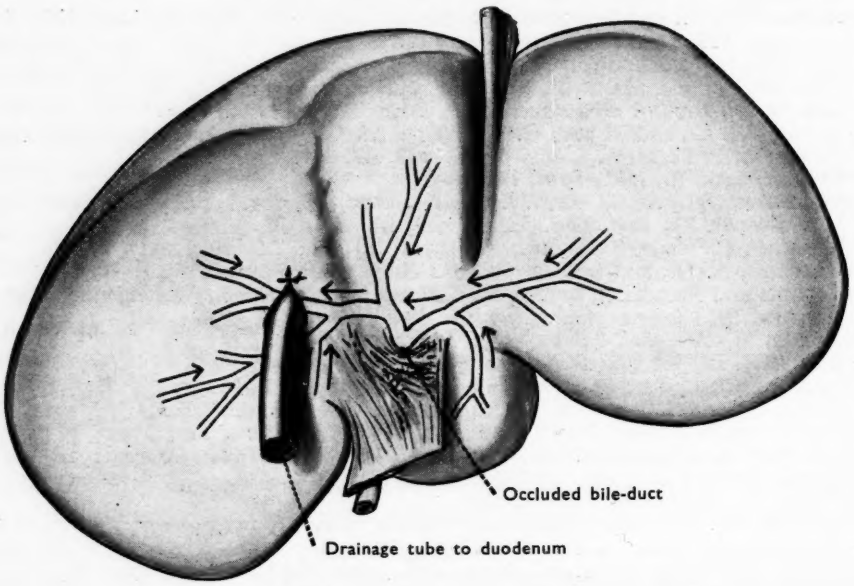


Fig. 318.—Drawing showing how the bile will flow out of a dilated duct in the right lobe when it is drained in cases of obstruction to the common hepatic duct.

in the recorded cases, a small portion of the liver has been excised so as to leave a raw area on which the bile-ducts opened. An incision was then made into the antimesenteric surface of a loop of jejunum and the edges of the incision were joined to the margins of the raw surface of the liver.

It is not until a surgeon is faced with a difficult problem that he commences to think seriously about it, and when I was confronted with such a case the practicability first occurred to me of placing a drainage tube into the liver so as to drain some of the larger ducts and connect the tube with the duodenum. At that time I had no idea that if obstruction to the common hepatic duct occurred at the transverse fissure of the liver and a large duct were drained from the right lobe, bile from the rest of the liver would drain away via this duct (*Fig.* 318). But this actually does take place.

The following is the clinical history of my case :—

Mrs. Mary J., aged 57, was admitted to hospital on February 10, 1938, complaining of right-sided abdominal pain of some two years' duration. The pain was intermittent and always commenced in the right upper abdominal quadrant and radiated round to the right scapula. The patient noticed a fullness and some flatulence after meals, which was relieved by belching. When the pain first commenced two years ago, there was some vomiting at times, but for the last year prior to admission this had not recurred. There was no history of jaundice and the pain did not bear any definite relation to meals. The bowels were regular and the motions were of a normal colour, and there was no history of any clay-coloured fæces. The patient had five healthy children and there was a history of two miscarriages.

On examination the patient proved to be an intelligent woman, well covered, and appeared quite healthy. The abdomen was lax and fat, and was generally somewhat tender on palpation. The maximum tenderness was in the right hypochondrium and Murphy's sign was positive. There was nothing abnormal in the urinary system.

It was decided to remove the gall-bladder, and the operation was carried out on February 11, 1938, under avertin and gas and oxygen anæsthesia. The abdomen was opened by a right paramedian incision, the rectus muscle being retracted laterally. On opening the abdomen dense omental adhesions to the anterior abdominal wall were found and divided. The gall-bladder itself was buried in adhesions which attached it to the anterior abdominal wall, the stomach, the first part of the duodenum, and the portal vein. These adhesions were divided, and the cystic duct which contained an impacted stone was dissected and clamped, together with an accessory duct passing from the right lobe of the liver into the cystic duct. The cystic artery was clamped and the gall-bladder dissected out of its fossa. Silk ligatures were applied to the cystic ducts and to the cystic artery, and the raw surface of the liver covered by approximating catgut stitches. A drainage-tube was inserted and the wound closed in layers.

The excised gall-bladder, which was very thickened, was devoid of mucous membrane in places, and contained four faceted stones of the infective type. The patient progressed well for the first week, after which a biliary fistula formed and bile drained copiously through the upper part of the incision for ten days. On March 6, 1938, cholangitis developed and the patient ran a high temperature (104°) for some days and had several rigors.

Jaundice appeared and the patient was treated with intravenous saline and cylotropine. The condition settled after a week and the biliary fistula lessened to a very slight discharge. The patient was discharged to her home on March 24, 1938, afterwards going to a convalescent home for a week.

The patient was re-admitted to hospital on May 28, 1938, because the biliary fistula had failed to heal and the stools were clay-coloured. There was general malaise and marked pruritus, together with considerable loss of weight. In spite of this her hæmoglobin was 104 per cent and the serum calcium 11·2 mg. per 100 c.c.

An X-ray examination after the introduction of lipiodol into the biliary fistula demonstrated the fact that a very slight amount of the opaque material entered the duodenum.

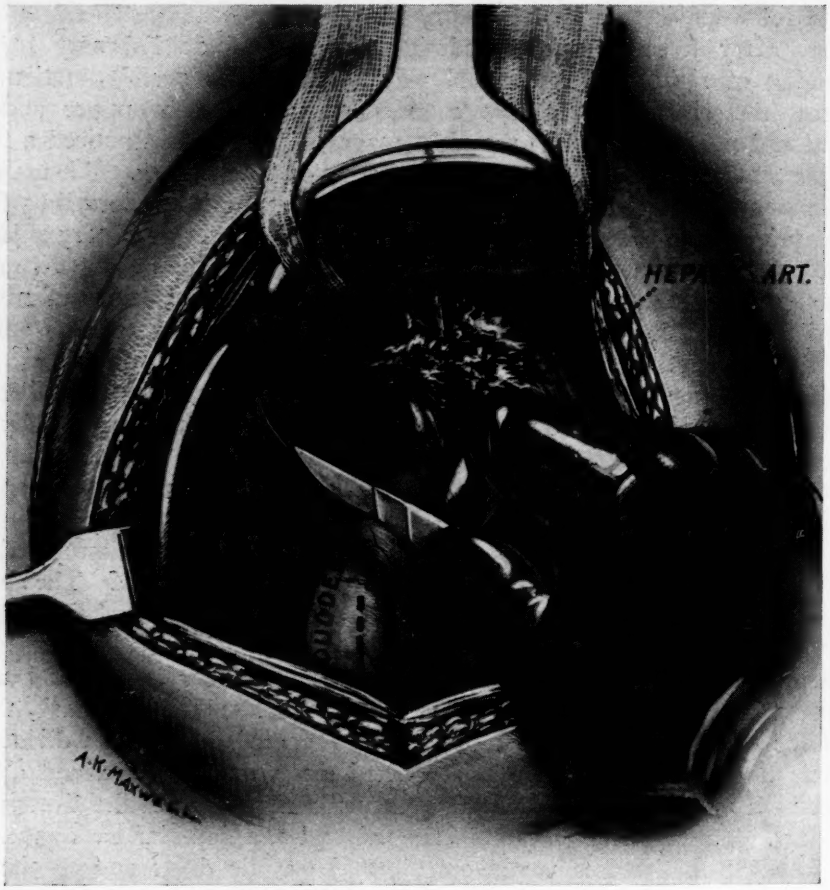


FIG. 319.—Drawing showing the position of the incision made into the under surface of the liver and the site of the duodenal opening.

As the patient's life was very miserable, a second operation was decided upon, and on June 1, 1938, the former scar, together with the biliary fistula, was completely excised. Dense fibrous adhesions were found surrounding the whole length of the supraduodenal portion of the common bile-duct. As much as possible of this dense fibrous mass was excised, the second part of the duodenum was opened, and a probe passed up the common duct from the papilla of Vater. The duodenum was closed and the abdominal wall was sutured in layers; a drainage tube being inserted down to the common bile-duct. Progress was unsatisfactory and the patient still continued to pass bile; she was discharged to a convalescent home

on June 28, 1938. She gradually became more jaundiced and suffered from marked itching of the skin. However, she did not want any further operative treatment and remained in the country until her condition became intolerable, when she begged for something else to be done to relieve her misery.

She was re-admitted to hospital on December 8, 1938, in a very poor condition. She was deeply jaundiced and there were multiple hæmorrhagic spots in the skin. Itching was so bad that the patient even scratched her skin while she was asleep.

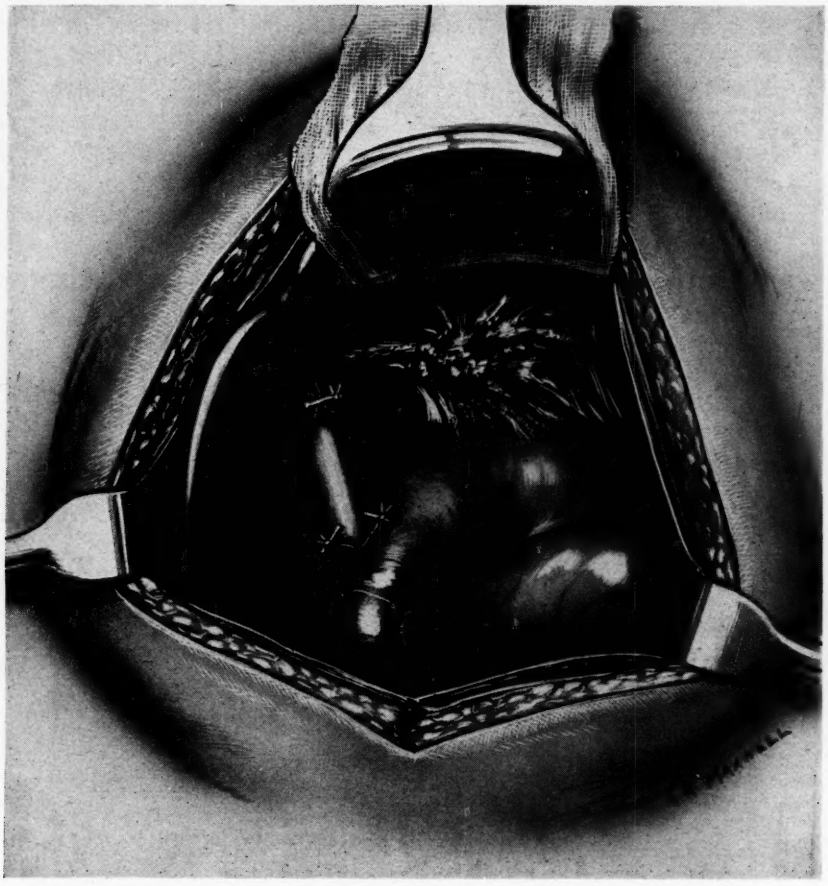


FIG. 320.—Position of the drainage tube in the liver and duodenum.

The bowels were very loose and the motions were clay-coloured. The urine was "like stout" and contained a large amount of bile-salts. The liver was enlarged and hard and protruded three finger-breadths below the costal margin. The conjunctivæ and the whole skin were jaundiced; the bleeding time was three minutes. The heart was dilated and many extrasystoles could be heard. Blood-pressure 110/65. The van den Bergh reaction gave a direct positive. The blood-count was as follows:—

Red blood-corpuscles	3,580,000 per c.mm.
Hæmoglobin	74 per cent
Colour index	1·03
Total leucocytes	9,400 and c.mm.

The patient was given large amounts of glucose; diathermy pads were placed in front and at the back of the liver, and diathermy treatments given every day for ten days.

A third operation was performed on December 30, 1938, under gas and oxygen anæsthesia. The whole of the abdominal scar, including the biliary fistula, was completely excised, and the abdomen explored through a 7-inch right paramedian incision. Many dense adhesions were present in the region of the transverse fissure of the liver, stomach, and duodenum. After a prolonged and careful

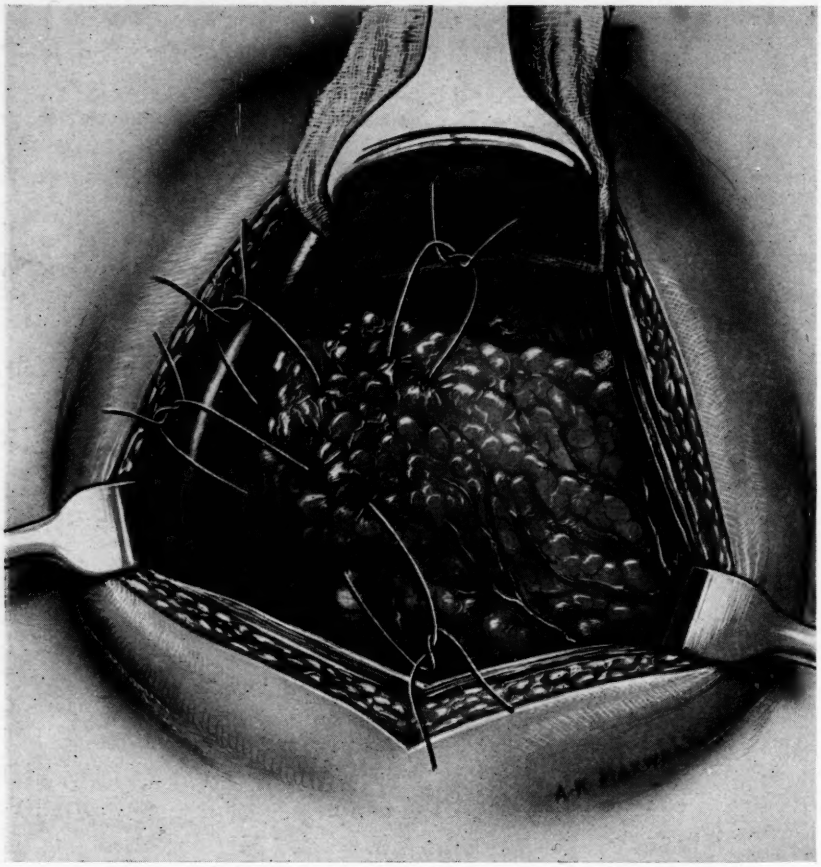


FIG. 321.—A large omental graft covering the hepatico-duodenostomy.

search for the common bile-duct, it was found to be a shrunken and collapsed cord below the liver, from which no bile could be aspirated by a syringe. An attempt was made to find a dilated common hepatic duct, but without success, although the region of the transverse fissure of the liver was explored with a syringe.

As there was no possibility, surgically, of removing the obstruction to the common bile-duct, and as the patient's condition was desperate, a hepatico-duodenostomy was performed. An incision was made on the inferior surface of the right lobe of the liver (*Fig.* 319). This incision was deepened to a depth of

two-and-a-half inches. Into the hole thus formed a large drainage tube was inserted and retained in situ by a catgut stitch. An incision was then made into the second part of the duodenum and the other end of the drainage tube was inserted into the duodenum through the opening thus formed, and retained there by two stitches (*Fig.* 320). The edges of the duodenal opening were then stitched to the liver and the anastomosis strengthened by carefully oversewing omentum (*Fig.* 321). The abdominal wall was closed in layers, and a peritoneal drain inserted for 48 hours. No bile was discharged from the wound after the drain was removed, and in three weeks the wound was soundly healed. The jaundice gradually disappeared and bile-pigment appeared in the stools. The liver diminished in size and the patient lost her intense itching and became a cheerful individual again. She was discharged from hospital on February 7, 1939, with the rubber tube still not passed. When seen on August 14, 1939, she was feeling better than she had done for years.

It is because of the bad prognosis in these cases of hepatico-duodenostomy that this case appears worthy of record.

NOTES ON A SUCCESSFUL CASE OF KRUKENBERG'S OPERATION

By THOMAS PURCE, Bindura, S. Rhodesia

Being very interested in an article on two successful cases of Krukenberg's 'Tong' operation[1], I have been on the look-out for a suitable case upon which to perform it. Recently a male native was brought into hospital suffering from a severe injury of the left hand sustained by being mauled by a leopard. The hand was so badly lacerated that there was difficulty in getting large enough flaps to make an amputation at the wrist-joint possible. I performed the amputation and left it to heal up for two weeks. I then performed the Krukenberg operation.

The forearm was split up for a length of 8 inches. Tendons and muscles were separated into two groups and the tendons were stitched to the periosteum and over the ends of the radius and ulna respectively. The muscles attached to the radius were the flexor pollicis longus, flexor carpi radialis, palmaris longus, a portion of the flexors digitorum sublimis and profundus, a part of the extensor digitorum communis, and the extensors carpi radialis longus and brevis. To the ulna were attached the extensor and flexor carpi ulnaris, the remaining portion of the flexors digitorum sublimis and profundus, and part of the extensor digitorum communis. The raw areas were covered with whole skin-grafts. The grafts took fairly well and healing occurred without any trouble, except that it was rather delayed in the angle of the limbs.

I was curious to see how well this man could use his forceps, as his age of 50 years was rather against the education of a new movement. He co-operated very well and was using the arm long before healing took place. In opening the limbs of the forceps an equal amount of abduction and supination of the radical limb takes place. Adduction occurs combined with pronation of the radial limb. The ulnar limb may be regarded as the fixed one. He can voluntarily open the limbs

to a distance of 2 in. at the peripheral ends (*Fig.* 322). The muscles which open the forceps are the supinator, brachioradialis, and the extensor and flexor carpi ulnaris.

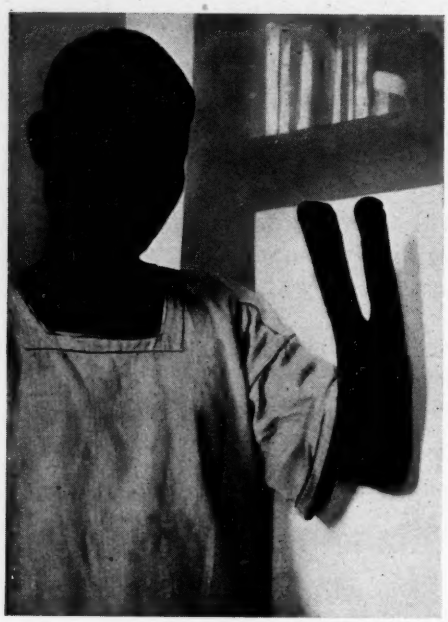
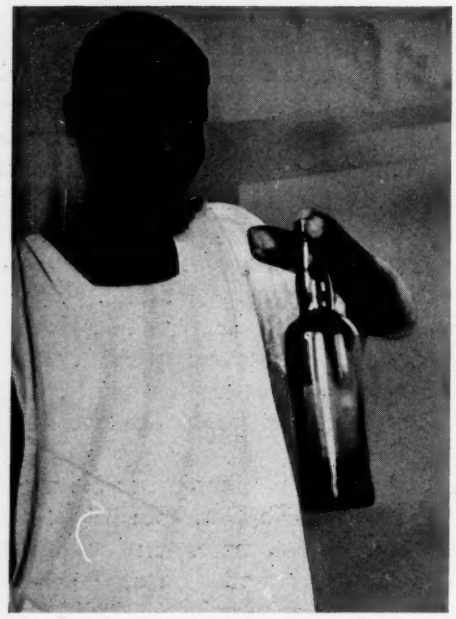
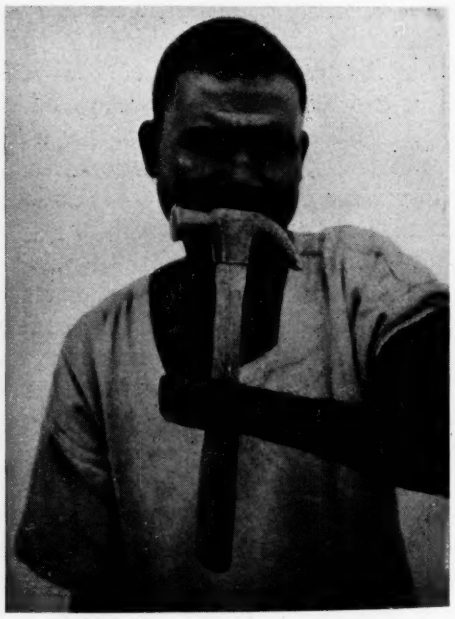


FIG. 322.—Showing the degree of opening of the forceps possible.





FIGS. 323, 324.—Showing how successfully a bottle and a hammer can be held.

The muscles giving the gripping power are the pronator teres, flexor carpi radialis, and to a slight extent the flexors digitorum sublimis and profundus. He can hold such things as a hammer or a bottle and can easily hold a knife or fork (*Figs.* 323, 324). I anticipate that with continual use and education he will find his forceps quite useful.

Commentary.—

1. This operation has a definite place in surgery on natives who for the most part are unable to afford prosthetic appliances.

2. It is possible to get a good functional result even in a fairly elderly patient, and age, within limits, should not debar a suitable case from the benefits of the operation. To make a success, however, it is essential to select the type who will give the necessary co-operation, otherwise the result will be a failure. The operation does not appear to be widely known, as I have found only one other reference in the literature[2] and the authors describe it as consisting of multiple operations.

I am indebted to Dr. A. P. Martin, the Medical Director, for permission to publish these notes.

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STRANGULATION OF AN INGUINAL HERNIA FROM AUTO-REDUCTION EN MASSE*

BY H. R. I. WOLFE
ASSISTANT IN THE SURGICAL UNIT, CARDIFF

As is well known the forcible manipulation of an inguinal hernia may sometimes result in displacement of the entire sac, with its contents still unreduced, out of the inguinal canal. The term ' reduction en masse ' is applied to this state, and where it has been produced by the patient's own manipulative efforts the term ' auto-reduction en masse ' has been applied (Walsham and Grey Turner). The condition may sometimes present a difficult surgical problem because naturally in such patients the hernia, although no longer palpable in the inguinal canal, may remain strangulated in the abdominal cavity; or if not actually strangulated at the time of reduction, may later become so; and the surgeon has to depend almost entirely on the patient's own story to guide him in making a diagnosis.

The following is an account of a case of this kind :—

HISTORY.—An ice-cream vendor, aged 36, was admitted to the Surgical Unit of the Cardiff Royal Infirmary on Christmas Day, 1938. He gave a history of having developed a cold with a dry cough three days previously. During a severe bout of coughing at 2 a.m. on the day of admission he experienced a sudden pain in the epigastrium, followed by vomiting. The pain, which was localized and of a gripping twisting nature, was agonizing and almost continuous. He experienced several rigors

* From the Surgical Unit, Welsh National School of Medicine, Royal Infirmary, Cardiff.

and vomited on four occasions. The vomit was at first undigested food and later "just clear water". He thought the attack was due to flatulence and forced his bowels to open at 4 a.m., when he passed a small motion but no flatus. The pain got worse, and he was seen by Dr. T. Wallace at 8 a.m. He was then in great pain and his cries could be heard in the street, but although the patient was writhing in agony nothing abnormal was found on physical examination. He was admitted to hospital one hour later.

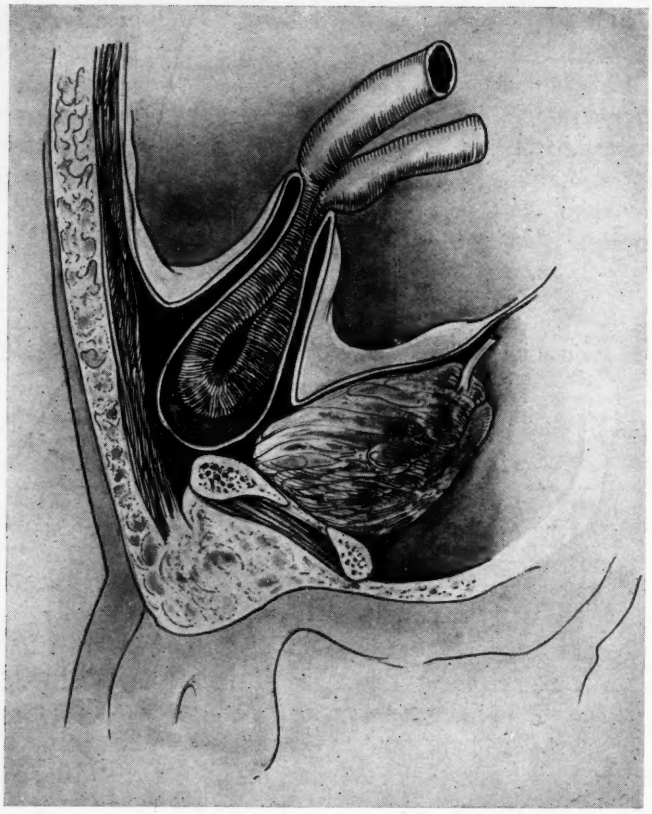

FIG. 325.—Diagrammatic representation of the condition found at operation.

Past History.—His left leg was amputated 18 years previously for a tuberculous knee-joint. Shortly after this operation he developed a left scrotal hernia. It was controlled by an elastic belt and the contents were easily reducible, except on one occasion 15 years ago when a doctor had to be summoned. A right inguinal hernia developed 10 years ago. This was "just a bulge noticed especially on coughing" and was easily controlled by a belt. Two months prior to admission, when doing some heavy lifting, the belt slipped and he experienced a pain in the groin. He found the hernia had increased in size. Reduction which he carried out himself was difficult and required some force, and was followed by abdominal pain and nausea. The pain was localized to the umbilical region and tended to radiate to the left side of the chest. The hernia had not reappeared since, and he had experienced no trouble up to the present time.

ON ADMISSION.—He was not in obvious pain. He had a left scrotal hernia the contents of which were easily reducible. The right inguinal canal was empty and not tender. The abdomen moved well on respiration: there was no distension or rigidity. There was slight tenderness in the umbilical region. Rectally there was no tenderness and nothing abnormal to be felt. His tongue was moist but slightly furred. Temperature 98·4°. Pulse 84. Respiration 22. Urine contained no abnormal constituents.

For the first 24 hours while in hospital he had twinges of pain, and on the evening of the next day vomited slightly. The pain was not severe and the temperature and pulse remained normal. An enema gave a poor fæcal result and no flatus was passed. The following day further vomiting occurred and a slight rise in the pulse-rate.

OPERATION.—Professor Lambert Rogers decided to perform laparotomy and this was carried out under general anæsthesia. The abdomen was opened by a right paramedian incision. A mass about 3 in. long was found in the lower abdomen and was at first taken to be an intussusception, but closer inspection proved it to be an invaginated hernial sac containing a loop of strangled gut and omentum (*Fig.* 325). The contents could not be reduced by manipulation, but on dividing the neck of the sac reduction was easy. The bowel and omentum were viable. The neck was sutured and obliterated and the abdomen closed.

Convalescence was uneventful and he was discharged 18 days later. He has since been re-admitted and had radical cure of both herniæ performed.

Comment.—The history suggests that auto-reduction had taken place two months prior to his final attack of strangulation. The patient had a 10-year old hernia which had been easily and painlessly reducible and controlled by a truss. On the occasion of a strain two months before admission, the hernia had increased in size and reduction was both difficult and painful. He himself succeeded in reducing it, however, and it did not reappear in the canal nor did he have any more trouble until the severe bout of coughing on the morning of admission. At operation an invaginated inguinal hernial sac was found containing strangulated gut and omentum. Auto-reduction *en masse* had presumably taken place two months previously and a severe bout of coughing had determined the onset of strangulation.

The condition is rare, for there are only 3 other similar cases in the literature. In Walsham's second case the interval between reduction and strangulation was two months, while in Professor Grey Turner's the interval was one of several months. In a recent review of the literature, H. E. Pearse has reported a third case where the interval was three weeks.

I am indebted to Professor Lambert Rogers for encouraging me to publish this case.

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PERINEAL EXCISION OF THE RECTUM

PROLAPSE OF BLIND END THROUGH A PERINEAL SINUS, WITH PARTIAL STRANGULATION 5½ YEARS LATER

By Sir CHARLES GORDON-WATSON

A MAN, aged 69, was operated on in June, 1933, for carcinoma of the rectum. A perineal excision was performed after a preliminary colostomy and nine inches of bowel removed. The upper cut end was invaginated and closed. There was a deposit of carcinoma in one gland only, two inches above the upper edge of the growth.

The closed blind end subsequently became patent and gradually prolapsed to the skin margin, and a permanent perineal sinus resulted causing a mucous discharge. This was followed some time later by intermittent prolapse of the mucosa, which was easily reducible.

In October, 1938, there was a sudden increase of prolapse, which became irreducible, congested, and painful. The prolapsed portion was removed and the

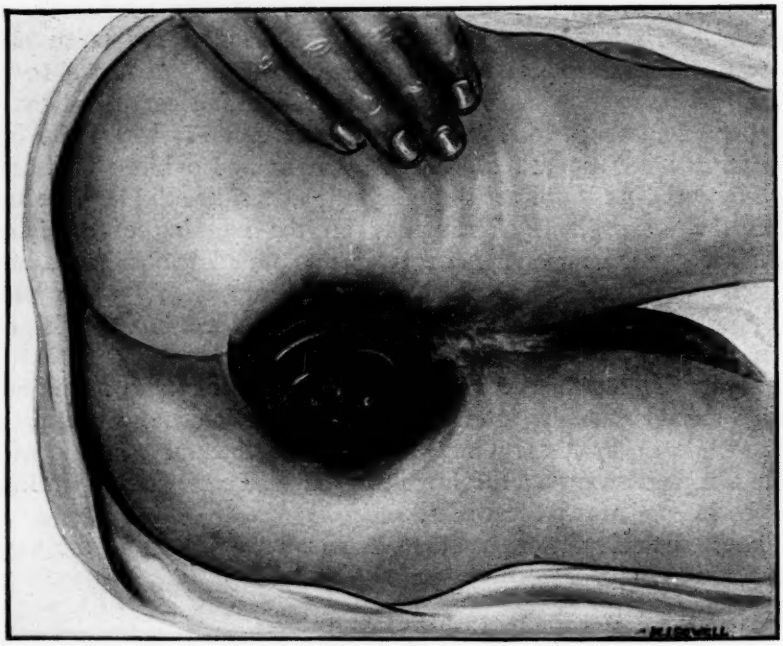

FIG. 326.—A drawing of the condition made at the time of operation.

blind end re-invaginated and closed. The coloured sketch (*Fig.* 326) was made at the time of the operation.

The case is recorded as being rare, if not unique.

BRONCHO-BILIARY FISTULA FOLLOWING STENOSIS OF COMMON BILE-DUCT

By I. DOUGLAS MILLER, Sydney

The following are notes of a remarkable case of broncho-biliary fistula resultant upon an injury to the common bile-duct. As most broncho-biliary fistulæ are the result of hydatid infestation of the liver with intraduct rupture, such a diagnosis was made in this case in spite of the patient's many operations on the biliary system.

History.—A male, aged 52, had received his previous treatment in the country. For about four years he had suffered from severe attacks of pain in the right hypochondrium. He had been subjected to various operations for this complaint.

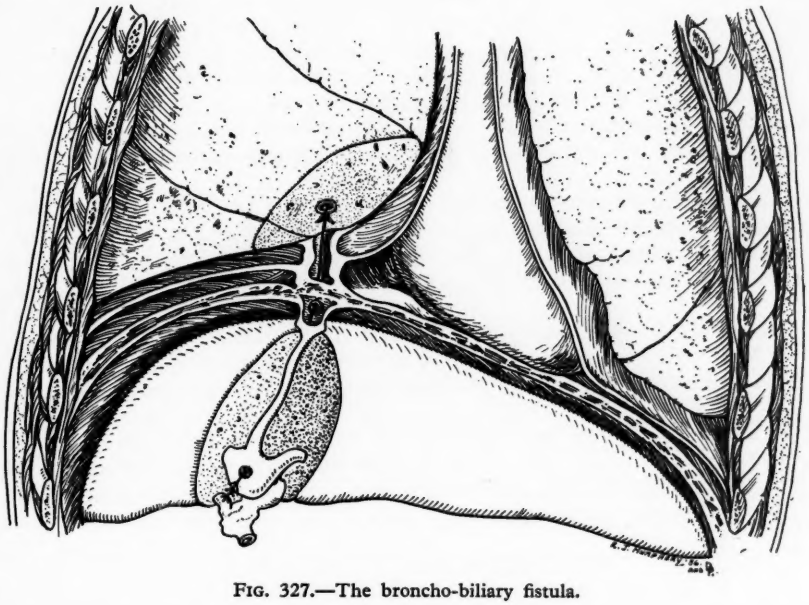

Fig. 327.—The broncho-biliary fistula.

About four years ago a gastro-enterostomy was done; three years ago a cholecystostomy; two years ago a cholecystectomy. The first two operations were apparently followed by some relief. After the cholecystectomy he obtained no relief, and the operation was followed by very intense pain and intermittent jaundice, which in six weeks became complete, after a few weeks was relieved, but again became complete.

Five months ago, when he was completely jaundiced and experiencing great pain, he suddenly coughed up a large quantity of bile. This coughing up of bile continued, and the jaundice passed off. Since this time he was racked day and night by an incessant cough, expectorating 60 oz. of bile in twenty-four hours. He became extremely emaciated. Lipiodol injection into the trachea failed to show the fistula.

Operation.—Under local anæsthesia, the diaphragm was exposed below the pleural reflection, after removing the tenth rib on the right side, and a dissection

carried out between diaphragm and pleura until just to the right of the midline a small strand of adhesions was divided. The fistulous track was enclosed within these. His cough stopped, and bile drained externally.

Two days later, owing to his very weak condition, a blood transfusion was performed. He suffered a very severe reaction and died.

PATHOLOGY (*Fig.* 327).—There is a cicatricial obliteration of the hepatic duct at the porta hepatis. Proximal to this the ducts are enormously dilated. A small fistulous track leads from one of these dilated ducts to the upper surface of the liver, and then through the diaphragm into the lung. This track was divided at operation.

REVIEWS AND NOTICES OF BOOKS

A Short Text-book of Surgery. By C. F. W. ILLINGWORTH, M.D., F.R.C.S. Ed., Lecturer in Clinical Surgery, University of Edinburgh; Senior Assistant Surgeon, Edinburgh Western Hospital. Second edition. 9¼ × 6 in. Pp. 707 + x, with 12 plates and 189 illustrations in text. 1939. London: J. & A. Churchill Ltd. 21s. net.

THERE is a persistent demand by students for short text-books of surgery. The difficulty which confronts the author is to condense so elaborate a subject within a reasonable compass and to decide how far the process shall go. The popularity of this book shows that the author has very successfully solved this difficult problem. His book covers the whole range of surgery, and the space devoted to different subjects has been skilfully and judicially apportioned. This new edition is quite up to date. It has extremely few omissions. But we should have liked to see some mention of the protective immunization against tetanus with toxoid, and the recommended prophylactic dose of serum would be thought by many to be inadequate.

If there is any criticism to be made it is that the author includes unreservedly all modern methods and suggestions without attempting to assess their real value. For example, such debatably unsound operations as presacral neurectomy and intraspinal injection of alcohol should have more than mere mention, which gives the impression that they are universally acceptable procedures.

Such subjects as blood transfusion are well and simply described, but the author's statement that the "hæmoglobin content is an accurate index of progress of blood loss" is not true. Before adjustment can take place the hæmoglobin estimation gives a deceptively favourable picture of the situation.

In the treatment of stone impacted in the ureter the reader cannot find the definite indications for undelayed operative removal.

Such criticisms as these are nevertheless minor ones, and a thorough search is required to find even these small blemishes in an otherwise excellent small manual.

A Textbook of Surgery. By American Authors. Edited by FREDERICK CHRISTOPHER, B.S., M.D., F.A.C.S., Associate Professor of Surgery at Northwestern University Medical School; Chief Surgeon, Evanston (Illinois) Hospital. Second edition. 9¾ × 6¼ in. Pp. 1695 + xxiv, with 752 illustrations. 1939. London: W. B. Saunders Co. 42s. net.

IT is not surprising that a new edition of this attractive text-book has been called for. A certain amount of revision has been carried out, so that it is thoroughly up to date. It is a remarkable editing feat to control the output of approximately 180 contributors so that uniformity in presentation is preserved. It is only to be expected that some sections would stand out in particular, but the average standard is high. There are features which are not usually so well presented in English text-books of this size, such as an excellent account of painful affections of the lower back. Other clear and satisfactory sections are those on the thyroid and on peptic ulcers. Curiously enough in both cases the authors have evaded giving precise information upon certain most important matters; in the one the criteria of operability in exophthalmic goitre are not defined, and in the other there is great lack of decision in the choice of operative treatment for duodenal ulcer. Again, in such a large treatise where many rare conditions are described at length, it would seem that tuberculous disease of the kidney would merit having more than two pages devoted to it; and a common operation such as

suprapubic prostatectomy might also receive fuller treatment, whilst the perurethral method could with advantage have been discussed at greater length. We could not find mentioned conservative resection of the rectum for carcinoma with restoration of continuity, a procedure which has received increased attention during recent years.

It would not be fair to this good text-book to give the impression that the defects are either numerous or serious; they are in fact very few, and the general level of presentation of the subject is very high. The book is attractive and easy to read, and well illustrated. By our standards it is a little large for the average undergraduate.

A Manual of Reparative Plastic Surgery. By J. EASTMAN SHEEHAN, M.D., F.A.C.S., Professor of Plastic Reparative Surgery, New York Polyclinic Medical School and Hospital; Surgeon, St. Clare's Hospital, etc. 9¼ × 6 in. Pp. 311 + xxiv, with 314 illustrations and 18 plates. 1938. London: Humphrey Milford, Oxford University Press. 30s. net.

THIS volume by Dr. Sheehan is offered "as a statement of the services to be had from the tissues of the body and as a compendium of information covering many varieties of surgical intervention with a view to plastic repair". It is an unsatisfactory book. At its best in discussing cosmetic problems of the face, it fails entirely to give an adequate account of the principles and practice of general reconstructive surgery. It is disappointing to find in every chapter an absence of the detailed instruction that is so necessary to success in this subject, and it is surprising in a book where brevity is apparently the aim to find so much irrelevant and wordy discursiveness. The book is not wide enough for those seeking instruction nor detailed enough for the expert, and its deficiencies are many. To mention just a few: the very important principle of the dimensions of a tubed pedicle flap is not discussed; there is no indication of how surgery and radium are to be combined for keloid scarring; there is generalization only on the treatment of burns and burn scars; the diagrams of forehead pedicle flaps are very misleading; the indications for use of a nerve-graft in facial palsy are so inexact as to be useless; and it is impossible not to protest at the so-called physiology of nerve repair and nerve-grafting.

This volume does not uphold the good opinion that the author's work on the nose and orbit had earned for him.

Plastic Surgery. By ARTHUR JOSEPH BARSKY, M.D., D.D.S., Associate Surgeon in Charge of the Department of Reconstructive Surgery, Beth Israel Hospital, New York City, etc. 9¼ × 6 in. Pp. 355, with 432 illustrations. 1938. Philadelphia & London: W. B. Saunders Co. 26s. net.

THIS book by Dr. Barsky succeeds much better than the one reviewed above in conveying the principles and practice of modern plastic surgery. It is a book of instruction for the practising surgeon and gives an adequate technical description of the methods and operations mentioned. The author has attempted to present the best operation for each of the conditions described, and although one cannot always agree with his choice, in general the method is a success. The book covers the whole field of general reconstructive work, and the plan which has been adopted of presenting photographs of case records immediately following diagrams illustrating the method employed is illuminating.

The author is at his best in discussing treatment of the conditions most commonly encountered in a general hospital—severe burn scarring, loss of tissue by injury, and facial injuries and fractures. The book is less satisfactory in discussing certain special conditions. Anyone with experience of the results of the operation performed by Veau, Wardill, and Kilner for cleft palate cannot possibly agree with the author's treatment of this condition. It would be difficult to plan the treatment of a case of facial palsy on the information made available by the author, and similarly difficult to effect a cure of keloid scar. The description and illustrations of protheses for use in connection with intrabuccal grafting are disappointing, and although cosmetic nasal surgery is well described, reconstructive surgery of the nose is very briefly mentioned and the description of the method is inadequate. The orbit receives better attention. But on the problems of skin, cartilage, and bone transplantation and the

general problems of plastic surgery the work is a reliable and valuable manual of instruction, and those working or seeking to work in this subject will find much of guidance and encouragement.

The Treatment of Fractures. By CHARLES LOCKE SCUDDER, A.B., Ph.B., M.D., F.A.C.S., Consulting Surgeon to the Massachusetts General Hospital; formerly Assistant Professor of Surgery at the Harvard Medical School. Eleventh edition, revised. 9½ × 6¼ in. Pp. 1208, with 1717 illustrations. 1938. Philadelphia and London: W. B. Saunders Co. 55s. net.

FOR its eleventh edition this standard work has been largely rewritten. In this important task the author has enlisted the aid of a number of collaborators, who have contributed some excellent chapters on various special subjects—most notably epiphysial injuries, pathological fractures, and injuries of the intervertebral discs. Dr. Scudder's well-known leanings towards the operative treatment of fractures is even more stressed than before, and the large number of illustrations of screws, plates, and other devices for internal fixation makes certain parts of the book resemble a surgical instrument catalogue. The author, no doubt, has tried to do justice to the large army of surgical inventors in this field, and the inevitable result is that he has included methods which are of ephemeral value. This distorted perspective is particularly seen in the account of the modern treatment of fractures of the neck of the femur, where an elaborate description is given of a method of internal fixation which few experienced fracture surgeons would be induced to adopt. In other chapters, however, sound principles are clearly defined as in the earlier editions, which have gained for this book its well-deserved reputation.

Gross Anatomy. A Brief Systematic Presentation of the Macroscopic Structure of the Human Body. By A. BRAZIER HOWELL, Associate Professor of Anatomy, Johns Hopkins University School of Medicine. 9¾ × 6⅝ in. Pp. 403 + vii, with 56 illustrations. 1939. New York and London: D. Appleton-Century Co. Inc. 25s. net.

THE time allocated in the curriculum of the average American medical student for the study of the structure of the human body has been reduced in recent years to such an extent that it is impossible for him, without some assistance, to grasp in the limited time at his disposal the essential facts of human gross anatomy. The standard text-books are filled with a mass of detail, the relative importance of which is not indicated except by the rather unsatisfactory method of printing in different type faces. To make a selection from this mass of facts is very difficult for a man who is not acquainted with his anatomical needs in medicine and surgery. Dr. Howell has written this book as an introduction to anatomy, and in it has selected those anatomical facts which every medical student should know. It makes no claim to completeness, but one can say that its value for a first-year student of anatomy is great. Dr. Howell suggests that the book be used in association with a standard atlas of anatomy and the dissecting-room work.

Physiologie et Pathologie du Tissue osseux. By RENÉ LERICHE, Professeur au Collège de France. 10 × 6½ in. Pp. 459, with 65 illustrations. 1939. Paris: Masson et Cie. Fr. 100.

THE election of René Leriche to the Chair of Medicine in the Collège de France will one day be regarded as a conspicuous landmark in the onward progress of surgical science. In the first year of his tenancy of a Chair adorned in previous generations by such masters as Claude Bernard and Brown-Séquard, Leriche has given a series of lectures in which he has traversed the whole realm of the physiology and pathology of bone. These lectures are now available in the form of a monograph which will still further enhance—if that were possible—the outstanding position which the author occupies in the world of surgery to-day. In each chapter, in characteristically brilliant and rhetorical style, Leriche is seen at its best, and the whole work makes delightful reading. His well-known and much challenged view on the formation

and behaviour of bone are set out again in even more convincing fashion. To illustrate his arguments, almost every type of bone disease comes under discussion. The thesis throughout is supported by observations drawn from a rich store of clinical experience, and from a long series of animal experiments in which the author has enjoyed the collaboration of a number of his devoted pupils.

Die Wintersportverletzungen. By Dr. MARCO PETITPIERRE, St. Moritz. $9\frac{3}{4} \times 6\frac{1}{4}$ in. Pp. 194, with 197 illustrations, some coloured. 1939. Stuttgart: Ferdinand Enke. RM. 17; bound, RM. 18.60.

THIS monograph gives a useful, if conventional, description of the more important injuries sustained in the various forms of winter sport—ski-ing, skating, ice hockey, and so on. The most original feature of the book is the excellent account of the mechanism of ski-ing injuries, illustrated by admirable diagrams.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers.]

Die Geschwülste in der Chirurgie. By Professor Dr. HERMANN COENEN, Münster. With an Appendix on *Die Zysten* by Doz. Dr. HANS HELLNER, Münster. Being a part of Bd. II of *Die Chirurgie* (Kirschner and Nordmann). Second edition. 10⅜ × 7¼ in. Pp. 176, with 198 illustrations. 1939. Berlin and Vienna: Urban & Schwarzenberg. RM. 9.

Die Chirurgie des Halses. By Professor Dr. BURGHARD BREITNER, Innsbruck. Being a part of Bd. IV of *Die Chirurgie* (Kirschner and Nordmann). Second edition. 10⅜ × 7¼ in. Pp. 152, with 85 illustrations and 1 coloured plate. 1939. Berlin and Vienna: Urban & Schwarzenberg. RM. 9.

Infections of the Hand. By L. R. FIFIELD, F.R.C.S. Eng. Second edition, by PATRICK CLARKSON, F.R.C.S. Eng., Surgical Tutor, Guy's Hospital; Demonstrator of Anatomy and Operative Surgery, Guy's Hospital Medical School. 7¼ × 4¾ in. Pp. 168 + xii, with 57 illustrations, including 8 plates (2 coloured). 1939. London: H. K. Lewis & Co. Ltd. 9s. net.

The Tissues of the Body. An Introduction to the Study of Anatomy. By W. E. LE GROS CLARK, F.R.S., Dr. Lee's Professor of Anatomy in the University of Oxford. 9¾ × 6½ in. Pp. 372 + xi, with 109 illustrations. 1939. London: Oxford University Press. 15s. net.

Treatment of some Common Diseases (Medical and Surgical). By Various Authors. Edited by T. ROWLAND HILL, M.D. Lond., M.R.C.P. Lond., Physician to the Southend General Hospital; etc. 8⅝ × 5½ in. Pp. 398 + xv, with 90 illustrations, including several in colour. 1939. Edinburgh: E. & S. Livingstone. 15s. net.

Pioneers in Acute Abdominal Surgery. By ZACHARY COPE, B.A., M.D., M.S. Lond., F.R.C.S. Eng., Surgeon to St. Mary's Hospital, Paddington; Senior Surgeon to the Bolingbroke Hospital, Wandsworth Common. 7⅜ × 4⅞ in. Pp. 134 + xii, with 38 illustrations. 1939. London: Oxford University Press. 7s. 6d. net.

Textbook of General Surgery. By WARREN H. COLE, M.D., F.A.C.S., Professor of Surgery, University of Illinois College of Medicine; and ROBERT ELMAN, M.D., Associate Professor of Surgery, Washington University School of Medicine, Saint Louis. Second edition. 9½ × 6⅛ in. Pp. 1031 + xxviii, with 559 illustrations. 1939. New York and London: D. Appleton-Century Co. Inc. 40s. net.

Surface Anatomy. By W. E. ROBERTS, M.R.C.S., L.R.C.P., Hon. Demonstrator of Anatomy, University of Sydney. With a Foreword by A. N. BURKITT, M.B., B.Sc., Professor of Anatomy, University of Sydney. 9 × 5¾ in. Pp. 93 + x, with 40 Plates. 1939. London and Sydney: Angus & Robertson Ltd. 7s. 6d. net.

Les Pièges de la Chirurgie en Diagnostic et Therapeutique. Erreurs ou Fautes ou Faits présumés tels. Conditions et Limites de la Responsabilité. By Professor E. FORGUE and Professor AIMES. 9½ × 6½ in. Pp. 510. 1939. Masson et Cie. Broché, Fr. 90; Cartonné toile, Fr. 120.

Synopsis of Surgical Anatomy. By ALEXANDER LEE MCGREGOR, M.Ch. Edin., F.R.C.S. Eng., Lecturer on Surgical Anatomy, University of the Witswatersrand; Assistant Surgeon, Johannesburg General Hospital. With a Foreword by Sir HAROLD J. STILES, K.B.E., F.R.C.S. Edin. Fourth edition. 7¼ × 4⅞ in. Pp. 664 + xx, with 648 figures. 1939. Bristol: John Wright & Sons Ltd. 17s. 6d. net.

Operative Orthopedics. By WILLIS C. CAMPBELL, M.D., Memphis, Tenn. 9½ × 6½ in. Pp. 1154 + xix, with 845 illustrations, including 4 coloured plates. 1939. London: Henry Kimpton. 55s. net.

Rectal Surgery. A Practical Guide to the Modern Surgical Treatment of Rectal Diseases. By W. ERNEST MILES, T.D., F.R.C.S. Eng., Senior Surgeon to the Gordon Hospital for Cancer, Fistula, and other Diseases of the Rectum. 8 × 5½ in. Pp. 359 + xi, with 2 colour plates and 105 illustrations. 1939. London: Cassell & Co. Ltd. 17s. 6d. net.

Clinica Quirurgica en las Hidatidosis Costal y Pleural. By PEDRO D. CURUTCHET, Buenos Aires. 8½ × 6 in. Pp. 182, with 39 illustrations. 1939. Buenos Aires: El Ateneo.

Guy's Hospital Reports. Edited by Sir ARTHUR HURST, D.M. Vol. LXXXIX (Vol. XIX, Fourth Series, No. 2, April, 1939). 9½ × 6 in. Pp. 121–249. Illustrated. 1939. London: Headley Brothers. Issued quarterly. Single numbers 10s. net; Annual subscription 30s. net.

Manual of Urology. By R. M. LE COMTE, M.D., F.A.C.S., Professor of Urology, Georgetown University Medical Department. Second edition. 9 × 6 in. Pp. 295 + v, with 55 illustrations. 1939. Baltimore: The Williams & Wilkins Co. (London: Ballière, Tindall, & Cox). 18s. net.

Sclerosing Therapy. The Injection Treatment of Hernia, Hydrocele, Varicose Veins and Hæmorrhoids. Edited by FRANK C. YEOMANS, M.D., F.A.C.S., Professor of Proctology and Attending Surgeon, New York Polyclinic Medical School and Hospital. 10 × 7 in. Pp. 337 + xii, with 117 illustrations. 1939. London: Ballière, Tindall & Cox. 27s. net.

Nitrous Oxide–Oxygen Anæsthesia. McKesson-Clement Viewpoint and Technique. By F. W. CLEMENT, M.D., Director of Anæsthesia at Flower Hospital, Toledo; etc. 9¼ × 6 in. Pp. 274, with 70 illustrations. 1939. London: Henry Kimpton. 18s. net.

Treatment of War Wounds and Fractures, with Special Reference to the Closed Method as Used in the War in Spain. By J. TRUETA, M.D., late Director of the Department of Surgery, General Hospital of Catalunya, Barcelona. With a Foreword by ERNEST W. HEY GROVES, M.S., F.R.C.S., Emeritus Professor of Surgery, Bristol University. 7¼ × 5 in. Pp. 143 + xiii, with 48 illustrations. 1939. London: Hamish Hamilton Ltd. 8s. 6d. net.

Thomson and Miles' Manual of Surgery. By ALEXANDER MILES, M.D., LL.D., F.R.C.S. Ed., Consulting Surgeon, Royal Infirmary, Edinburgh, and Sir DAVID WILKIE, Late Professor of Surgery, University of Edinburgh. Ninth edition. 8½ + 5⅜ in. In two volumes: Vol. I, General, pp. 1–656, with 346 illustrations; Vol. II, Regional, pp. 657–1371, with 298 illustrations. Each volume contains the complete index to the two volumes. 1939. London: Oxford University Press. 21s. net each volume.

Surgical Diagnosis. By STEPHEN POWER, M.S. (Lond.), F.R.C.S. (Eng.), Assistant Surgeon, London Homœopathic Hospital; Surgeon, Eltham Hospital. 8⅜ × 5⅜ in. Pp. 228 + viii, with 51 illustrations and 15 plates. 1939. Bristol: John Wright & Sons Ltd. 12s. 6d. net.

Sidelights on the Life of a Wearside Surgeon, 1859-1938. By WILLIAM ROBINSON, M.D., M.S., F.R.C.S. Eng., Hon. D.Ch. Durham. 8½ × 5½ in. Pp. 154. 1939. Gateshead-on-Tyne: Northumberland Press Ltd. 5s. net.

The Study of Anatomy. Written for the Medical Student. By S. E. WHITNALL, M.A., M.D., B.Ch. (Oxon.), M.R.C.S., L.R.C.P., F.R.S. (Canada), Professor of Anatomy in the University of Bristol. Fourth edition. 7¼ × 4⅞ in. Pp. 124 + viii. 1939. London: Edward Arnold & Co. 4s. 6d. net.

Recent Advances in Anæsthesia and Analgesia (including Oxygen Therapy). By C. LANGTON HEWER, M.B., B.S. (Lond.), D.A. (R.C.P. & S. Eng.), Anæsthetist and Demonstrator of Anæsthetics, St. Bartholomew's Hospital; etc. Third edition. 8 × 5¼ in. Pp. 333 + xii, with 132 illustrations. 1939. London: J. & A. Churchill. 15s. net.

St. Bartholomew's Hospital Reports. Edited by G. EVANS, G. GRAHAM, G. HADFIELD, C. F. HARRIS, J. MAXWELL, W. SHAW, A. WORMALL, Sir G. BALL, J. P. ROSS, and R. V. CHRISTIE. Vol. LXXII. 8½ × 5½ in. Pp. 375 + xxviii. Illustrated. London: John Murray. 21s. net.

Cancer of the Colon and Rectum: Its Diagnosis and Treatment. By FRED W. RANKIN, M.A., M.D., Sc.D., F.A.C.S., Surgeon, St. Joseph's and Good Samaritan Hospitals, Lexington, Kentucky; and A. STEPHENS GRAHAM, M.D., M.S., F.A.C.S., Surgeon, Stuart Circle Hospital, Richmond, Va., and Associate Professor of Surgery, Medical College of Virginia. 10 × 6½ in. Pp. 358 + x, with 133 illustrations. 1939. London: Baillière, Tindall & Cox. 30s. net.

Artificial Limbs and Their Relation to Amputations. 9⅝ × 6 in. Pp. 88, with 42 illustrations (22 plates). 1939. London: H.M. Stationery Office. 3s. net.

Anæsthesia: Narcosis; Local; Regional; Spinal. By A. M. DOGLIOTTI, M.D., Professor of Surgery, University of Modeno. Authorized English Translation by CARLO S. SCUDERI, M.S., M.D., F.A.C.S., Associate in Surgery, University of Illinois, College of Medicine. 10¼ × 7 in. Pp. 680 + xx, with 236 illustrations, some coloured. 1939. Chicago, Ill.: S. B. Debour. $7.50.